Cosmetic Potential of Natural Products: Industrial Applications

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Abstract

The cosmetic industry is a high-valued and evergreen multibillion dollar industry with more specialized and advanced products adding up every year. The major product categories in the cosmetic industry are skin care, hair care, perfumes, deodorants, toiletries, and make-up. Of these, skin care products top the list, accounting around 36 % of the global cosmetic market. Natural products, a treasure of medicinally active compounds are used for treating various skin ailments, infections, inflammation and as a protectant of UV irradiation and pollution. The hybrid of cosmetic and pharmaceutical compounds, known as cosmeceuticals, possesses therapeutic as well as beautification potential based on its key ingredients. Natural products are well regarded as a rich source of cosmeceuticals. Different classes of natural compounds originating from animal, plant, and marine algal sources are placed under the category of high-valued cosmetic ingredients. The extraction of fatty acid components from botanicals and other natural sources opens up a big market in the cosmetic industry. The present chapter introduces the recent advancement and strategies followed in the cosmeceutical industry, and the role of plant tissue culture in enhancing the production of pharmaceutically valued natural products along with the current regulatory policies.

Keywords

Biotechnology · Cosmeceuticals · Phytochemicals · Natural products · Regulatory policies

10.1 Introduction

We are living in an era of increasing air pollution. The efforts of the scientific community and increased evidences of pollution-induced morbidity and mortality worldwide have created the awareness among people on the detrimental effect of pollutants on the skin (Juliano and Magrini 2018). Once considered as the extravaganza, and as an ingredient among the elite class, cosmetics for skin and hair care are now used widely to enhance health and beauty. The trend of using cosmetics as a positive healing aid started from such awareness and eventually led to the beginning of the fastest-growing cosmetic sector, also known as "cosmeceuticals." Even though the practice of pharmaceutically active cosmetics was started in early and medieval era (Oricha 2010), the field of cosmeceuticals was initially conceptualized by the US cosmetic chemist Raymond Reed in 1961–1962 and later popularized by an American dermatologist, Albert Kligman, by around 1970. Cosmeceuticals are the hybrids of cosmetic and pharmaceutical molecules or preparations that are intended to improve the beauty and health of the skin. According to Kligman (2000), cosmeceuticals are the topical applicants, which come under the broad spectrum of pure cosmetics and pure drugs. Basically, cosmeceuticals are the cosmetic products that can improve appearance, delivering pharmaceutically valued nutrients for a healthy skin. Accordingly, almost all of the cosmeceutical products are intended for skin care, hair care, and antiaging activities. Rather than visualizing as products that camouflage the irregularities in appearances, cosmeceuticals are regarded as the natural or synthetic chemicals that can offer protection, rejuvenation, and healing capabilities (Verma et al. 2016).

Spice extractives, like those from ginger, pepper, cinnamon, mint, and bio-active food ingredients like milk peptides, plant-derived nutrients, oils from medicinal plants, and certain minerals and vitamins, are all now better utilized as cosmeceuticals. This recent trend has increased the face value of an array of natural products and also has unravelled the pharmaceutical benefits of historically used natural cosmetics. Most of the cosmetic manufacturers are presently active in the cosmeceutical industry, with some targeting to the specific personal care products. Antiaging cosmeceuticals encompass a major market share with a wide range of functional properties attributed by natural ingredients with soothing, healing, and rejuvenating potential. Natural products with good antioxidant and anti-inflammatory effects are high valued in applications, like post-procedural inflammation reduction (Wisniewski et al. 2014). The usual search for noninvasive and nonsurgical methods to tackle aging effect ended up in choosing the antiaging topicals, which are more acceptable due to "natural and organic" labels. Bio-active peptides and lipid compounds with inherent antiaging properties have made a mark as alternative to compounds like BOTOX that functions by lifting and smoothing aged skin. Matrixyl, the trade name of a combination of palmitoyl pentapeptide-3, and its variants are best examples for skin stimulating peptide-fatty acid combination.

Aside from having a legal responsibility by a company or individual on the safety and labelling of the cosmetic product, agencies, such as the Food and Drug Administration (FDA), USA, do not have any legal authority in approving the efficacy of the product before its launch in the market (Lohani et al. 2014). Because of that, cosmeceuticals have to undergo safety tests but not the efficacy tests. Efforts are initiated to improvise the rules and regulations to establish industry standards pertaining to quality control. In accordance with the increase in demand and market trend, cosmeceutical research is gaining value in industrial arena. The present chapter introduces the recent advancement and strategies followed in the cosmeceutical industry, and the role of plant tissue culture in enhancing the production of pharmaceutically valued natural products along with the current regulatory policies is also discussed.

10.2 Natural Products as Cosmetics

Pharmaceutically active cosmetic ingredients from the natural sources top the list of newly launched cosmeceutical products, basically due to the consumer acceptance and comprehension on the reduced side effect and high efficacy. A lot many firms are active in evaluating the cosmeceutical efficacy of an identified natural product or to discover a novel molecule from various natural sources.

10.2.1 Herbal Products

Herbal constituents are the most explored and valued in cosmeceutical industry as they are less allergic and toxic (Joshi and Pawar 2015). Cosmetics containing herbal products has gained wide acceptance among consumers worldwide during the past few years. Herbal products may be used in the crude form or after processing depending upon the purpose of use. Herbal ingredients are widely used in skin care and hair care formulations and dental products. Based on phytochemical nature, herbal cosmetics are categorized into carbohydrates, resins and tannins, glycosides, fats, oils and waxes, essential oils, and alkaloids.

10.2.1.1 Carbohydrates

Carbohydrates containing natural products are mainly used in cosmetics as emollient, emulsifying agents, suspending agents, and dental adhesives. The carbohydrate-containing herbal drugs that are used as emollient include acacia gum (*Acacia senegal*), tragacanth (*Astragalus gummifer*), and ispaghula (*Plantago ovata*). Acacia gum, guar gum (*Cyamopsis tetragonolobus*), and tragacanth, a natural gum attained from the dried sap of plant species of the genus *Astragalus*, including *A. adscendens*, *A. tragacantha*, *A. gummifer*, and *A. brachycalyx*, are used as emulsifying agent, as suspending agent, and as stabilizer in lotions and protective creams (Viinanen et al. 2011). The common dandelion (*Taraxacum officinale* L.) contains the polysaccharides, TOP1 and TOP 2, which show the activity against oxidative stress and can be used in preparing skin care formulations (Park et al. 2014). *Arundinaria gigantea* Muhl. is a natural source of silica used in skin care and anti-aging formulations (Lu and Liu 2003). Wild oats (*Avena sativa*) boost ceramide synthesis through the activation of peroxisome proliferator-activated receptor (PPAR) and are used as moisturizers in cosmetic preparations (Chon et al. 2015). *Triticum vulgare* extract contains oligosaccharides which promote tissue repairing in vivo and in vitro (Sanguigno et al. 2015). *Ceratonia siliqua*, *Astragalus cicer*, *Astragalus propinquus*, and *Caesalpinia spinosa* are used in skin care cosmetics and contain galactomannans which can stimulate inherent collagen synthesis and inhibit matrix metalloproteinase (MMP) expression (Prajapati et al. 2013). Alpha hydroxy acids like citric acid (citrus fruits), malic acid (apple), and glycolic acid (grape wine) are used in anti-wrinkle preparations (Smith 1996; Thibault et al. 1998). Alpha hydroxy acid present in sugarcane extracts (*Saccharum officinarum*) is a common constitutent of skin care cosmetics. Okra (*Abelmoschus esculentus*) may be used to extract mucilage which has considerable emulsifying capacity. It was also used in skin care preparations to reduce the dryness (Archana et al. 2013). Likewise, the rhamnogalacturonans from okra can be applied to increase cell renewal in the skin (Deters et al. 2005).

10.2.1.2 Resins and Tannins

Resins are complex amorphous products produced by plants with wide application in cosmetic industry. Colophony (a solid form of resin) from *Pinus palustris* mainly contains resin acids like abietic acid and have the potential to be used as stiffening agent in ointment. Myrrh (*Commiphora molmol*) is a resin-containing drug (commiphoric acid) and is used as ingredient in tooth powder and mouth wash (Oktemer et al. 2015). Tannins are the secondary metabolites of plants, mainly used as astringent and antiseptic in skin care preparations. A tannin-containing drug, myrobalan (*Terminalia chebula*), which is used in dental preparations has the ability to inactivate microbial adhesions, enzymes, and cell envelope transport proteins (Prakash and Shelke 2014). The antioxidant, antiviral, antifungal, and antibacterial properties of amla (*Emblica officinalis*) have been exploited in various hair care preparations like oils and shampoos. *E. officinalis* was proved to be protecting the skin cells from UV radiation by reducing the oxidative stress (Majeed et al. 2011). Bearberry contains phytochemical constituents like arbutin, quercetin, gallic acid, and ellagic acid which have proven astringent action. Phenolic compounds extracted from oak (*Quercus robur*) is effective as topical antioxidant and has good absorption in ultraviolet B radiation range (Morteza-Semnani et al. 2003; Geetha and Roy 2012). *Arnica montana* which contain phenolic compounds and flavonoids may be used in skin care preparations (Ho et al. 2016). Sugarcane (*S. officinarum*) may be used as a good source of antioxidants which contain compounds such as gallic acid, chlorogenic acid, and ferulic acid (Feng et al. 2015). Polyphenols from baobab (*Adansonia digitata*) is used in skin care formulations especially antiaging cosmetics. Peach (*Prunus persica*) is used in the cosmeceutical formulations meant for antiaging, exfoliation, and regeneration of the skin and in hair care preparations (Abbasi et al. 2010). Peach also contains compounds with significant antioxidant activity like gallic acid, protocatechuic acid, protocatechualdehyde, chlorogenic acid, p-coumaric acid, and ferulic acid (Loizzo et al. 2015). Dog rose (*Rosa canina* L.) improves cell life and delays age-related skin changes (Phetcharat et al. 2015). *Rosa damascena* contains quercetin, kaempferol, and ellagic acid, which can inhibit tyrosinase enzyme activity and can be used in ointments against hyperpigmentation of the skin (Solimine et al. 2016).

10.2.1.3 Glycosides

The key component responsible for the biological activities of glycosides is sugars (Chao et al. 2008). The glycosides with significant cosmetic potential include aloe (*A. vera*, *A. barbadensis*, *A. africana*, *A. spicata*), fenugreek (*Trigonella foenum-graceum*), and bearberry (*Arctostaphylos uva-ursi*). Various phytochemicals extracted from aloe such as aloin, aloe emodin, barbaloin, and dihydrocoumarin derivatives showed antioxidant activity and provide protection from UV light (Yen et al. 2000; Hamman 2008). *Aloe vera* is used in various cosmetics including moisturizing cream, sunscreen products, and shampoos. The plant extract of fenugreek (*T. foenum-graceum*) was found to be effective in shampoos used to eradicate lice from hair (El-Bashier and Fouad 2002). Khan and Abourashed (2010) showed that licorice (*Glycyrrhiza glabra*) was effective in dermatitis and possesses antiseptic and antibacterial activity. Licorice is also reported in promoting hair growth (Upadhyay et al. 2012). Vanilla (*Vanilla planifolia* and *V. tahitensis*) may be used to stimulate hair growth (Nanda et al. 2010). Ginseng (*Panax ginseng*) is used as antiaging agent in cosmetics. Hwang et al. (2017) proved that ginseng can inhibit wrinkle formation and increases the moisture content of the skin. Mucilage extracted from *A. digitata* is used as suspending agent and as a natural excipient in cosmetics (Deshmukh et al. 2013). Turmeric (*Curcuma longa*) prevents the formation of wrinkles and hyperpigmentation of the skin and may be used in creams, lotions, and face packs (Sumiyoshi and Kimura 2009).

10.2.1.4 Fats, Oils, and Waxes

Ceramides, cholesterol, and fatty acids are the major components of stratum corneum, which is the major barrier for drug absorption. The chemical nature of the skin and sebum promotes the usefulness of fats, oils, and waxes as skin care products. Almond oil (*Prunus dulcis*) contains phenolic compounds with free radical scavenging potential and is reported to be effective against pimples (Pinelo et al. 2004; Milbury et al. 2006; Rao 2012). Almond is also used as emollient in cosmetics. The hydroxytyrosol present in olive oil (*Olea europaea*) possesses great cosmetic potential as raw material (Miralles et al. 2015). Olive oil is used as demulcent, emollient, and pharmaceutical aid in industry. Linoleic acid in castor oil (*Ricinus communis*) will get integrated into the skin and reinforces the skin (Patel et al. 2016). Castor oil is used as ointment base and main ingredient of lipstick in cosmetic industry. Persic oil (*Prunus armeniaca*) is used as pharmaceutical aid in industry. Persic oil protects the skin from ultraviolet radiation and is used in the preparation of scrub, cream, lotion, face wash, and oil in cosmetic industry (Raj et al. 2012). Jojoba oil (*Simmondsia chinensis*) is used as emollient and pharmaceutical aid. The high oil content, long shelf life, and low moisture content made it suitable for use in industry as cosmetic base. It has high saponification number which makes it useful for formulating soaps, shampoos, conditioners, moisturizers, shaving creams, etc. (Sandha and Swami 2009). Sesame oil (*Sesamum indicum*) is used as antioxidant, demulcent, and emollient and for curing pimples (Prasad et al. 2012). Kokum (*Garcinia purpurea*) contains glycerides of stearic acid, oleic acid, and palmitic acid. Kokum is also used as ointment base in cosmetic industry (Ranveer and Sahoo 2017). Theobromine in cocoa butter (*Theobroma cacao*) scavenges the reactive oxygen species generated in the skin as a result of UV exposure and has higher antioxidant capacity than tea and red wine (F'guyer et al. 2003). Cocoa butter is used as emollient, lubricant, and base for suppository and ointments in pharmaceutical industry (Ash and Ash 2007). Cocoa increases the blood flow to the skin and improves skin texture (Kim et al. 2011).

10.2.1.5 Essential Oils

Essential oils are fragrant principles isolated from the plants. Pine needle oil (*Pinus mugo*), rose oil (*Rose gallica*, *R. alba*, and *R. centifolia*), sandal wood oil (*Santalum album*), myrcia oil (*Pimenta racemosa*), and valerian oil (*Valeriana officinalis*) are used as perfumes in cosmetic industry. Orris oil (*Iris florentina*) is used as dentifrice in dental products (Olshan et al. 2000). Volatile oils extracted from tea tree (*Melaleuca alternifolia*), thyme (*Thymus vulgaris*), lemon grass (*Cymbopogon citratus*), oregano (*Origanum vulgare*), rosemary (*Rosmarinus officinalis*), calamint (*Calamintha officinalis*), and lavender (*Lavandula officinalis*) are used as natural preservatives in industry. Antimicrobial activity of *Thymus vulgaris* is attributed to thymol, carvacrol, γ-terpinene, or p-cymene (Juliano et al. 2000) and of *R. officinalis* oil to 1,8-cineole and α-pinene (Wang et al. 2012). Clove oil (*Eugenia caryophyllus*) has antioxidant and antimicrobial property and is widely used in pharmaceutical industry. *Achillea millefolium* L. is widely used in the cosmetic industry in skin care preparations. The essential oils were found to alter the melanin production by decreasing tyrosinase activity through the regulation of the JNK (c-Jun N-terminal kinase) and extracellular signal-regulated kinases (ERK) (Peng et al. 2014). *Artemisia abrotanum* and *White genepi*, belonging to the same genus, are used in the cosmetic industry as skin care products (Anthonavage et al. 2011). Safflower (*Carthamus tinctorius*) was found to have UV protective action and is used in sunscreen preparations (Kong et al. 2013). The seed extract of sunflower (*Helianthus annuus*) is included in hair care preparations (Guo et al. 2017). *Matricaria chamomilla* has antioxidant and UV-protecting effect and is used in the formulation of antiaging cosmetics (Jadoon et al. 2015). *Tagetes erecta* contains lutein which has UV-filtering effect and antioxidant activity (Siriamornpun et al. 2012) and is widely used in skin care products. *T. vulgaris* has protective effect against UV radiation and is used as a natural preservative in cosmetic products (Cornaghi et al. 2016). Rosemary extract (*R. officinalis*) is found to have antiaging potential attributed to its active ingredient carnosic acid (Calabrese et al. 2000; Birtić et al. 2015). Anthocyanins extracted from *Ocimum basilicum* possess antiandrogenic action and is used in anti-hair loss preparations (Kumar et al. 2011). A formulation of cinnamon with centella and tamarindus was proved to increase the moisture content and decrease the melanin content of the skin (Saraf et al. 2012).

10.2.1.6 Alkaloids

Alkaloids are the nitrogenous compounds of considerable medicinal and cosmetic value found in herbs. Alkaloid caffeine (*Coffea arabica*) which contains purine ring is used in alopecia associated with dihydrotestosterone (Fischer et al. 2007). *Styphnolobium japonicum* contains alkaloid oxymatrine which may be used to prevent keloid and deposition of collagen (Fan et al. 2012). The dihydrocoumarin isolated from *Melilotus officinalis* is used in cosmetics as antiaging preparations (Olaharski et al. 2005). Seeds of *Cola nitida* contain caffeine, theobromine, and theophylline which are found to be effective in preventing wrinkle formation and helpful in averting neutrophil infiltration caused by UV radiation (Mitani et al. 2007).

10.2.2 Marine Sources

Sea is splendid pool of enormous phytochemicals with cosmetic potential, currently in use and yet to be discovered. Apart from phytochemicals, sea is an immense treasure of bio-active compounds from marine algae, fishes, and underwater organisms. Spermaceti isolated from the head cavities of sperm whale (*Physeter macrocephalus*) contains hexadecyl esters like cetyl palmitate, cetyl laurate, cetyl myristate, and cetyl stearate. It is mainly used in ointments and creams in cosmetic industry (Carrier et al. 2002). Ambergris is a waxy substance insoluble in water obtained from sperm whale extensively used as perfume in cosmetic industry. Cod liver oil (*Gadus morrhua*) is a source of vitamin A, vitamin D, and glycerides of fatty acids and is prospective as emollient in cosmetic preparations. Macroalgae are the richest sources of phycocolloids. The phycocolloid agar and carrageenan are isolated from *Gelidium cartilagineum*, *Gracilaria confervoides*, *Chondrus crispus*, and *Gigartina mamillosa* (Botla et al. 2013). Algin is a phycocolloid of great value in cosmetic industry, mainly extracted from *Macrocystis pyrifera*. They are widely used as emulsifying agents, suspending agents, thickening agents, stabilizer, and gelling agents in the industry. The main characteristics of phycocolloids exploited in cosmetic industry include antioxidant, collagen boosting, anti-inflammatory, sunlight protection, UV absorption, melanin production inhibition, moisturizing, weight gain prevention, and antiviral and antibacterial properties (Farris 2010). The extracts from macroalgae are used for manufacturing cosmetics like creams, body lotions, soaps, shampoos, hair conditioners, toothpastes, deodorants, shaving creams, perfumes, and make-up items (Bowe and Pugliese 2014). Chitin and chitosan extracted from crustacean shells are widely used in cosmetic industry as antiaging agent, antioxidant, moisturizing agent, sunscreen, and skin protectant. It is used as a vehicle in toothpaste, mouth rinse, and dental varnishes and also finds application as a carrier for sodium fluoride, chlorhexidine, and herbal extracts in dentistry. Chitosan and its cationic derivatives interact with the hair keratin and increase the strength and softness of hair by forming elastic film over hair. It has been included in various hair care products like shampoo, hair spray, and hair tonics (Aranaz et al. 2018).

Sea cucumbers are marine invertebrates used to isolate a large variety of bioactive compounds with cosmetic potential such as sulfated polysaccharides, cerebrosides, chondroitin sulfates, lectins, sterols, peptides, and saponins. The extracts from sea cucumber varieties like *Apostichopus japonicus* inhibit the enzymes tyrosinase and tyrosinase-related proteins and have the potential to be used in skin whitening preparations. Sea cucumber-derived products find enormous application in industry such as cream, lotions, lipstick, gel, and sunscreen products (Siahaan et al. 2017). Kojic acid and azelaic acid extracted from fungi *Aspergillus* sp. and *Malassezia* sp., respectively, are used in skin whitening preparations. The marine fungi like *Botrytis*, *Pestalotiopsis* sp., and *Microsporum* sp. and marine bacterium *Thalassotalea sp.* possess compounds with the ability to inhibit tyrosinase enzyme. Marine fungal species like *Acremonium* sp., *Epicoccum* sp., *Aspergillus wentii*, and *Keissleriella* are promising natural resources of antioxidant compounds. Cosmeceutically active carotenoids are extracted from certain marine bacterial species under the genera, *Paracoccus* and *Agrobacterium*, and also from yeast species that come under genera, *Rhodotorula*, *Phaffia*, and *Xanthophyllomyces* (Corinaldesi et al. 2017). The marine carotenoids have remarkable antioxidant and ultraviolet shielding effect which can be utilized in formulating cosmetics.

10.2.3 Other Natural Sources

In this section, cosmeceutical compounds majorly from animal sources excluding marine origin are included. The exploration and utilization of animal products in cosmetics is limited by ethical, ethnical, and religious barriers. Honey is a viscous sweet secretion containing mainly glucose, fructose, sucrose, and dextrin and is sourced from honey bees (*Apis mellifera*). It is used to treat cracked lips and pimples. Commercially, honey is used as an ingredient in face wash, face packs, moisturizing lotion, scrub, and hair care formulations (Ediriweera and Premarathna 2012). Hydrous wool fat (lanolin) obtained from *Ovis aries* is used as absorbable ointment base. Beeswax obtained from *Apis mellifera* is utilized as ointment base and hardening agent. It is a constituent of cold creams, deodorants, depilatories, hair creams, hair conditioners, and eye cosmetics (Mishra et al. 2017). Botulinum toxin from *Clostridium botulinum* has the ability to prevent wrinkle formation by paralyzing the muscles for 3 to 4 months (Ramose-Silva and da Silva Carneiro 2007). Musk obtained from male musk deer belonging to family Cervidae is one of the most expensive perfume in the world. Muscone which is a muscopyridine is responsible for its cosmetic potential. Civetone obtained from civet, belonging to Viverridae family, is a high-priced fine perfume in cosmetic industry. Castoreum, a yellowish anal sac exudate of *Castor canadensis* (the North American beaver) and *Castor fiber* (the European beaver), and its derivatives are primarily utilized as fragrance in cosmetics and perfumery. Cochineal dye is deep crimson red in color extracted from the female cochineal insects (*Dactylopius coccus*). The red dye carminic acid is used in cosmetic industry as coloring agent in lipstick, eye shadow, and blush. Gelatin is produced by acid or alkali hydrolysis of the collagen extracted from the skin, bone, and connective tissues of mainly bovine and porcine origin. Collagen possesses good cosmetic value as it increases the moisture content of the skin and prevents wrinkle formation. It is used as an ingredient in many cosmetic products like cream, lotion, sunscreen, and hair care preparations (Rodriguez et al. 2018). Shellac is a mixture of resin and wax obtained from the insect, *Laccifer lacca*. It is widely used in nail polish to give glossy coating, which lasts for longer duration. Hyaluronic acid is a polysaccharide containing glycosaminoglycan, commercially prepared from animal tissues as well as from microorganisms like *Streptococcus*, *Bacillus*, and *Escherichia coli*. It has the ability to reduce scar and wrinkle formation and increases the moisture content of the skin (Olejnik et al. 2012). Summarizing the recent findings and observations in natural product research, the cosmeceutical value of natural products and formulations are augmenting along with the market value of cosmetic products. Imparting pharmaceutical value to the cosmetic components and ingredients has gained a considerable commercial gain in terms of the efficacy and consumer acceptance.

10.3 Value of Natural Products in Cosmeceutical Industry

As a latest addition to the cosmetic industry, cosmeceuticals are the fastest-growing sector with new product ranges being added to a plethora of premium brands. According to a report published in Research and Market Report in 2016, global market of cosmeceuticals will grow at a compound annual growth rate (CAGR) of 5.95% from 2017 to 2021. As per the "Asia Cosmetic Market Guide 2016" issued by US Department of Commerce, an annual growth of 10 to 20% is expected in the cosmeceutical industry. The Asian market comprises over 20% of US global export in cosmetic sector and offers over 3 billion consumers. Japan, South Korea, and Australia constitute a well-established cosmetic market that consumes products of over USD 1 billion from the USA. China, which imports US personal care and cosmetic products of USD500 to 600 million, is predicted to lead the list within the next 2–3 years (Asia Personal Care & Cosmetics Market Guide 2016). Increasing pollution and its awareness, rise in consumer income, and the change in lifestyles are the driving factors of global beauty care industry. It is estimated that the cosmetic industry generated a revenue of EUR178 billion at retail sales in Germany in 2012 (Kapoor and Si 2014). Still, the per capita levels of cosmetics in most countries are very low. Japan and South Korea, the major consumers of cosmetics in Asia, spend USD174 and USD171 per person per annum, respectively. Countries like China, Australia, and Vietnam have per capita levels of 24, 30.47, and 5.28 UD dollars, respectively (Asia Personal Care & Cosmetics Market Guide 2016).

Basically, cosmetic products are used for nourishment of skin and hair. Based on application, they can be classified under specific objectives such as antiaging, antiwrinkling, UV and cosmic ray protection, anti-acne, anti-allergic, and antioxidant. Advancement in our knowledge on skin physiology and aging led to identification of novel biological targets that can improve skin health and appearance. Appeal of natural products as safe and effective cosmeceutical ingredients led to immense researches and the identification of phytochemicals and marine compounds to be the part of the cosmetic formulations. Pharmaceutical industries mostly relay on the traditional medicine and knowledge database for developing new formulations and active molecules. Utmost importance and demand for such product lines exist in the skin care segment.

10.3.1 Skin Care Cosmeceuticals

Physiologically, the skin consists of two layers, i.e., epidermis and dermis. Epidermis is the outer barrier that gives physical and chemical protection to inner environment from external factors. The dermal layer is responsible for structural support. Stratum corneum, the outermost layer of epidermis, is cemented by a mix of triglycerides, free fatty acids, ceramides, cholesterol, cholesterol sulfate, and water (Tortora and Grabowski 2013). The external environmental factors that affect skin health are UV radiation, air pollution, stress factors, and natural aging process. Damages to the dermal layer, which constitutes about 90% of skin tissue, will result in wrinkles, flaccid skin surface, and stretch marks (Elias and Friend 1975). Cosmeceuticals do have more demand in skin care segment, because of their ability in moisturizing, cleansing, smoothing, and reinforcing the outer layer, which promotes the external appearance. In 2016, the major share of global cosmeceutical market was covered by skin care cosmeceuticals. Beiersdorf, L'Oréal, Shiseido, and Procter & Gamble are the key players manufacturing the skin care cosmeceuticals (Global Cosmeceutical Market 2017–2021, 2016).

Alpha hydroxy acids (AHAs) and β-hydroxy acids (BHAs) are fruit acids, which can reduce the signs of aging and to restore skin hydration by shedding outer layer of epidermis (Rivers 2008). Glycolic acids, citric acid, malic acid, lactic acid, tartaric acid, pyruvic acid, and mandelic acid are examples of AHAs. Of these, glycolic acid and lactic acid are the most commonly used acids. Mandelic acid and benzilic acid are phenyl group containing AHAs which can increase the lipophilicity compared to water-soluble AHAs. BHAs include salicylic acid, 2-hydroxy-5-octanoyl benzoic acid (LHA), and tropic acid. These are simple and complex aliphatic compounds which can act on ichthyosis- and xerosis-affected stratum corneum (Huber and Christopher 1977; Uhoda et al. 2005). Polyhydroxy acids (PHAs) are second-generation AHAs with more hydroxyl groups. They are naturally occurring metabolites which have additional benefits of imparting gentleness, hydration capacity, and antioxidant effect than AHAs. Compared to glycolic acid, gluconolactone, a PHA commonly used in cosmetic formulation, is compatible to sensitive skin and can strengthen skin barrier. The third-generation hydroxyl acids are aldobionic acids or bionic acids (BA), with a sugar molecule attached to PHA. They are synthesized enzymatically and are attached by an ether bond. Lactobionic acid and maltobionic acid are the two BAs with a high moisturizing potential. Compared to AHAs and PHAs, BAs are nonirritating, non-burning, and non-stinging (Green 2014; Green et al. 2016).

Retinoids are the commonly used natural cosmeceutical ingredients, which have antioxidant potential, and can prevent the photoaging. Commonly seen natural retinoids are retinol, retinal, and retinoic acid (Burke 2015). Retinoids are used clinically in treating squamous cell carcinoma, psoriasis, and acne vulgaris. Retinoids are approved by the FDA for the topical acne treatments. Retinoic acid is approved for treating fine skin wrinkle and liver spots. Retinol is a common ingredient in the cosmetic preparations as it is less irritant and can penetrate the epidermis easily (Aziz et al. 2017). The present trend of incorporating natural products with moisturizing, emulsifying, and maintenance of skin barrier homeostasis function is focused toward the use of botanicals. Accordingly, plant extracts and plant-based formulations became effective components in the modern cosmeceutical products. Compounds originated from plants and other sources that are presently used in the cosmetic industry are mentioned in the coming sections.

10.3.2 Hair Care Cosmeceuticals

Hair is a powerful indicator of health and personality for both men and women. Androgenetic alopecia (AGA) is the most common cause of hair loss in a gross 40% hair loss in women and 50% of men (Castelo-Soccio 2012; Banka et al. 2013). The three layers of hair shaft, cortex, medulla, and cuticle, are protected by the outermost layer, cuticle. This layer is responsible for hydrophobicity and can act as protective sheath to external stress factors. UV exposure, increase in reactive elemental species, harsh chemicals such as chlorine, heat stress, and hair treatment methods may lead to hair protein denaturation. Hair care products available in the market can be categorized into two – those which act on exocuticle (shampoo, conditioners, hair gels, etc.) and those which act on cortex (coloring agents, bleaching agents, and perming agents). Based on target regions, hair follicle can be divided into four – sebaceous gland, hair matrix cells, bulge region, and hair follicle infundibulum (Patzelt et al. 2008). So far, there are only two FDA-approved medication for hair loss – minoxidil and finasteride. Cosmetic industry is focusing more on including natural cosmeceutical formulations for effective treatment of hair loss (Madnani and Khan 2013). Common modes of action of plant-based compounds in promoting hair growth are by inhibiting 5α-reductase, transforming growth factor-β (TGF-β), protein kinase-C, and enhancing insulin growth factor-1 (IGF-1), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and fibroblast growth factor-2 (FGF-2) (Kwack et al. 2011; Herman and Herman 2016; Vañó-Galván and Camacho 2017).

Major class of hair care extracts are those from fruits that contain polyphenols with antioxidant activity. Clinical trials with 1% procyanidin B-2 from apple was carried out by Takahashi et al. (2001) and showed a 78.8% increase in mean value of hair diameter compared to placebo controls. Raspberry ketones isolated from raspberry is proved to be effective in promoting hair growth through activation of sensory neurons and increasing insulin-like growth factor 1 (IGF-1) levels (Ogawa et al. 2010). Caffeine is a methylxanthine class of compound, which can improve skin barrier function and phosphodiesterase inhibitory effect. Caffeine, when administered by follicular penetration, increased hair growth in human studies (Bansal et al. 2012). Isoflavones are chemical compounds with estrogen-like activity and are known as phytoestrogens. Inherently, such compounds have IGF-1-activating potential and can apparently enhance hair growth. Isoflavones also possess antiaging effect as evidenced by a human study which increased the epidermal thickness and collagen content in the skin (Neha et al. 2018). Green tea extracts are rich in polyphenols and contain the antioxidant molecule epigallocatechin gallate (EGCG) which is a 5-alpha reductase inhibitor. Researchers observed that the inhibition potential of EGCG enhanced after its esterification with palmitic acid (Rondanelli et al. 2015). White wax is a secondary metabolite from *Ericerus pela* Chavannes. About 93–95% of white wax is composed of monobasic saturated fatty alcohols and monobasic saturated fatty acids. Policosanol is the saturated monocyclic alcohol mixture extracted from white wax. A recent study has showed that policosanols can promote hair follicle growth compared to 2% finasteride in experimental mice (Wang et al. 2017). L-Ascorbic acid 2-phosphate, a vitamin C derivative, is experimentally proved to have hair shaft elongation activity compared to control samples (Kwack et al. 2010). Human placenta hydrolysate (HPH), a rich source of IGF-1 and amino acids, is a recent addition in hair loss therapy (No et al. 2015).

10.4 Impact of Biotechnology and Nanotechnology in Cosmeceutical Research

The term cosmeceutical is not valid so far under the rules of FDA. According to the rules and regulations imparted by FDA and European Regulation of Cosmetic Products (ERCP), the manufacturer should ensure safety of product before its launch in the market. It is not mandatory that these products should undergo efficacy test as they claim, but should not be adulterated or misbranded. Keeping pace with the demand of cosmeceuticals in the market, the manufacturers are forced to prove the potential of their product in terms of claim. Now, with the increasing impact of modern science among common people, the cosmetic consumers demand scientific proof for the real efficacy of ingredients (Fischer et al. 2015). A new trend of personalized skin care cosmeceutical regimen has emerged that are exclusively through physicians and rule out the possibility of online market sales (Lewis 2017). As cosmeceuticals are cosmetic products with pharmaceutical component, the curiosity for mode of action increased. A lot many cosmetic companies have invested to improve their genetic engineering, genomics, and proteomics facility to drive innovation in product development.

Plant cell culture techniques, biomimetic research, peptide engineering, and 3D bioprinting are the major supposed to be impact of biotechnology in cosmeceutical industry. In the field of antiaging creams and lotions, researchers were able to elucidate signaling pathways leading to antiaging gene activation. Developments in plant cell culture have led to the increased production of verbascoside, a phenylpropanoid glycoside which has better anti-inflammatory and antioxidant property (Vertuani et al. 2011). The oil-soluble extract from *Rubus idaeus* has been proved to enhance the expression of genes involved in skin hydration and moisturization (Tito et al. 2015). The permeation of active ingredients through skin barrier poses a major hurdle in the cosmetic industry. The introduction of nanotechnology in cosmetic industry enhanced the activity profile of existing ingredients massively. Broadly, nanotechnology has increased the efficacy and active transport of cosmeceutical compound through skin barrier. Controlled release of materials is another advantage of nanotechnology. Nanocomposite conjugated cosmeceuticals, or nanocosmeceuticals, are widely used in anti-wrinkle creams, sunscreen lotions, and skin whiteners due to its suitability in both lipophilic and hydrophilic surface. Nanocosmeceuticals possess an increased shelf life with stable product appearance and flow properties. Drug delivery methods using nanotechnology include hydrogels, nanoemulsions, liposomes, solid-liquid nanoparticles, smaller-sized nanoparticles, and dendrimers (Golubovic-Liakopoulos et al. 2011; Ganesan and Choi 2016). The incorporation of phosphatidylcholine, ceramides, and cholesterol to nanosized liposomes has increased the moisturizing and smoothening effect of skin care and hair care products. The use of phytochemicals in nanoscale in cosmeceutical preparations is increasing due to consumer acceptance (Katz et al. 2015). Liposomes incorporated with active compounds like retinols, vitamin E and K, ferulic acid, and antioxidant molecules like lycopene, carotenoids, and peptides showed an increase in physical and chemical stability even after dispersed in aqueous solution. Solid-liquid nanoparticles (SLNs) are nanosized colloidal carriers composed of biodegradable and physiological lipids with low-grade toxicity and also have more skin contact due to small size. This ensures enhanced occlusive property and skin hydration effect. Antiaging creams, such as Nano Repair Q10 cream and Nano Repair Q10 Serum launched by Dr. Kurt Richter Laboratorien GmbH, Germany, in 2005, authenticated the success of nanoparticles in cosmeceutical preparation. Due to the slow release potential of SLNs, these are also used as topical vehicle for perfumes.

Another type of nanomaterial used in the industry is nanocrystals. These are 10–400 nm size ranged particles used to deliver hydrophobic particles. The best example of nanocrystal-based delivery is of rutin glucoside. The study on human volunteers proved that a nanosuspension of 5% undissolved rutin was 25% more effective in photoprotection than 5% solution of water-soluble rutin glucoside. Another exciting class of chemical with nanoparticle functionality are dendrimers. Several patents have been filed by companies like the Dow Chemicals, L'Oreal, and Unilever on dendrimer-based hair care and skin care products (Furukawa et al. 2012; Kumari et al. 2017; Naha et al. 2018). Fullerenes are another class of synthesized nanoscale antioxidant material used in cosmeceutical industry for skin rejuvenation formulations. These are highly hydrophobic molecules consisting of odd-numbered carbon rings imparting a three-dimensional spherical structure. Research reports are inadequate to confirm the safety of fullerene particles in higher concentration even though it has been reported to be safe to use at lower concentrations in topical application. Zelens® Fullerene C-60 Day cream is a C-60 nanoparticle-based skin care cream from Zelens Ltd (Rigano and Lionetti 2016).

Advanced drug carriers based on nanotechnology have increased the scope of natural products and its activity profile in cosmetic arena. In other words, the cosmeceutical potential of such natural products got expanded when loaded to nanocarriers. An increase in surface area of nanosized synthetic complexes correspondingly enhanced the drug delivery through skin barrier, making it more efficient in antiaging and UV protection formulations. Skin retention and antioxidant potential of quercetin were enhanced upon SLN encapsulation (Han et al. 2014). Nano *Aloe vera* (Kitture et al. 2015), nano curcumin (Suwannateep et al. 2013), nano resveratrol (Yutani et al. 2015), nano lycopene (Riangjanapatee et al. 2013), and nano green tea (Gülseren and Corredig 2013) are a few nanosized phytochemical additions to cosmeceutical market. Advancement in cosmeceutical research and drug delivery strategies straight away results in new product entries from cosmetic giants. A few of them are listed in Table 10.1.

Table 10.1 New cosmeceuticals available into the markets

Product/brand name	Manufacturer	Key cosmeceutical	Category/ applications[a]
PROVOQUE™ Eye Complex	Aivita Biomedical, CA, USA	Alpha-2-HS-glycoprotein (fetuin)	Skin care, reduces under-eye skin wrinkles
PROVOQUE™ Facial Serum	Aivita Biomedical, CA, USA	Alpha-2-HS-glycoprotein (fetuin)	Skin care, targets wrinkles/fine lines, loss of firmness, texture, and discoloration
HydraTint	AlastinSkincare®, Inc. CA, USA	*Dunaliella salina* extract, *Camellia sinensis*, ergothioneine	Sunscreen lotion, UVA/UVB protection
Complexion Correcting Shield SPF 50+	Avène , USA	Vitamins E and C	Skin care, UVA/ UVB protection
Anaphase Shampoo	Ducray Laboratoires Dermatologiques, France	Tocopheryl nicotinate; vitamins B5, B6, and B8 (biotin); monolaurin; hydrolyzed wheat proteins; and ruscus	Hair care, hair loss supplement
Skin EssentiA® Antioxidant and Peptide Eye Gel	Environ Skincare, Australia	Blend of vitamins C and E, peptides, and low levels of vitamin A	Antiaging cream
Skin EssentiA® Botanical Infused Moisturizing Toner	Environ Skincare, Australia	Blend of plant extracts, vitamins, and antioxidants	Skin care, non-oily, pH balanced lotion
Daily Shield Lotion Tinted SPF 50	Episciences, Inc., USA	Blend of botanicals such as *Helianthus annuus*, *Argania spinosa*, *Rosmarinus officinalis*, *Pyrus malus*	Skin care, antioxidant, UV protection
Triple Defense Brightening Complex SPF30	Pierre Fabre Dermo-Cosmetique, USA	Epiwhite™ (a compound of essential amino acids and lipid residue), niacinamide, vitamin B3, marine algae complex	Skin care, moisturizer, UV protection
Hydra-Intensive Cooling Masque	iS Clinical®	Contains natural botanical antioxidants *Centella asiatica*, resveratrol, green tea, *Aloe vera*, and rosemary extract	Skin care, moisturizer, prevents sunburn
Hyaluronic Acid Boosting Serum	PCA Skin	Contains hyaluronic acid and sodium hyaluronate	Skin care, increase skin's innate hyaluronic acid production

(continued)

Table 10.1 (continued)

Product/brand name	Manufacturer	Key cosmeceutical	Category/ applications[a]
PRO Restorsea LipMagic™	Restorsea LLC, USA	Contains vitamin C, licorice leaf extract, soybean seed extract, and palm oil	Skin care cosmetic, improve lip appearance
Lytera 2.0 Pigment Correcting Serum	SkinMedica, USA	Contains tranexamic acid, phenylethyl resorcinol, niacinamide and tetrapeptide-30, a marine extract	Skin care, whitening effect

[a]As claimed by the manufacturer

10.5 Plant Tissue Culture for the Cosmeceutical Industry

Herbal cosmetics are in vogue today across the globe for beauty and personal care. Owing to the zero or petite side effects of natural contents in botanicals, which are known to enhance beauty as well as provide the body with nutrients, natural products and extracts from herbs have gained much popularity in the cosmetic industry. Laden with multifunctional biological activities enabling pharmaceutical value alongside beauty enhancement, inclusion of natural products in cosmetic formulations, which claim the therapeutic efficacy (now popularly called "cosmeceuticals"), is highly promoted by the cosmetic industry (Saha 2012). In contrast to the chemical and synthetic beauty products, which are known to give many harmful side effects, the herbal cosmetics with natural ingredients has been accepted by the end users for skin and body care without much apprehension. This has led to tremendous increase in the demand for herbal products for cosmetic preparation.

The natural products otherwise called the active principles are chemical compounds produced by plants during their metabolism and are known widely as secondary metabolites. These are synthesized and accumulated in various parts of the plant. Extracting these metabolites for a wide range of purposes using the traditional methods usually means destroying the plant diversity, since a large amount of biomass can yield only a meagre quantity of the metabolite in most cases. The escalating exigency for the metabolites in both pharmaceutical and cosmetic industry calls for improvised and alternative methodologies for natural product extraction and scale-up of production without deteriorating the biodiversity. Biotechnology is a prospective scientific discipline which provides ample opportunities for both production of biomass and the scale-up and extraction independent of the geographical and seasonal variations or the need for destroying the plants as such (Nosov 2012; Wilson and Roberts 2012). This can be accomplished by utilizing cells, tissues, organs, or the entire organisms by growing them in vitro or by genetically maneuvering them to obtain the desired metabolites (Rao and Ravishankar 2002). The major biotechnological approaches involved in secondary metabolite production include techniques in plant cell and tissue culture such as meristem/organ culture, cell/callus culture, and suspension cultures. Genetic transformation studies using *Agrobacterium* species (the natural genetic engineers) have also opened up new vistas for natural product biosynthesis especially using hairy root cultures. These technologies have facilitated the commercial production of a series of high-value natural products for food, pharmaceutical, and cosmetic industry (Fischer et al. 2015).

10.5.1 Tissue Culture for the Mass Production of Cosmeceuticals

Ever since Gottlieb Haberlandt (1902) predicted that plant cells are totipotent and there is possibility of multiplying the cells and thereof generate new plants, the world of "plant tissue culture" has grown into a new discipline. Across the years, the field of plant tissue culture has been put to use for mass propagation, clonal propagation, cell and tissue culture, and most importantly the production of natural products – the secondary metabolites which form the basis for most of the pharmaceutical and natural cosmetic preparations.

Metabolite production procedures involving microorganisms and animal cell cultures often need expensive and complex media formulations for the metabolic biosynthesis (Jeandet et al. 2013). Compared to the above systems, in vitro plant cell culture is a cost-effective and yet practical approach for the large-scale production of metabolites of cosmetic and pharmaceutical significance. Plant cell cultures need uncomplicated culture media comprising of base nutrients and minerals along with simple sugars and plant growth hormones for their growth and development. With this type of cultures, there is always a good prospect of sustainable and continuous metabolite synthesis (Donnez et al. 2009). It also offers opportunities for enhancing production using elicitor/precursor molecules as well as industrial scale-up using technologies like bioreactors.

10.5.1.1 Organ Cultures

Phytochemical synthesis and accumulation in plants are reliant on diverse factors. Tissue specificity of biosynthesis, growth, and differentiation stage of the plant, ecological and environmental parameters, and the season of growth usually influence the secondary metabolite production and yield of the extract. Cosmetic and pharmaceutical industry now has gained momentum with the upsurge of the demand for natural and organic formulations. In wake of this mounting plea for natural products, manufacturers are on the lookout for reliant and sustainable technologies for the large-scale synthesis and extraction of natural products.

Whole plant extracts seldom cater to the demand which correlated the synthesis of metabolites. To keep up with the requirement, a large quantity of biomass has to be sacrificed leading to dwindling in genetic diversity. To overcome these multitudes of challenges, scientists and manufacturers have started exploiting alternative and reliable tools utilizing the plant cell and organ cultures for sustainable production of useful phytochemicals (El Meskaoui 2013). Regenerating shoots have been found to be a better choice for phytochemical extraction compared to whole plant extract. Alkaloid content of *Fritillaria unibracteata* in vitro cultured shoots was found to be higher than the wild plant species (Gao et al. 2004). Likewise, the somatic embryos and the regenerating shoots of *Digitalis* sp. turned out to be a better producer of cardenolide-a cardiac glycoside. Culturing *Frangula alnus* on MS medium with naphthaleneacetic acid (NAA) (0.1 mg/l) and thidiazuron (TDZ) (0.1 mg/l) effected high rate of anthraquinone metabolite biosynthesis in vitro (Karuppusamy 2009).

Cosmetic industry also now relies upon the plant organ culture technique to ensure consistent supply of the active phyto-ingredients for their cosmeceutical formulations. Zerumbone, a metabolite used in skin whitening agent with antimicrobial properties, has been obtained from in vitro raised rhizome of *Zingiber zerumbet* organ culture method (Idris et al. 2007). Mahendranath et al. (2011) developed protocol for the production of annatto – the reddish orange pigment of *Bixa orellana* from normal root cultures. This has enabled the production of the cosmeceutically important pigment year long without depending on the availability of the aril from seeds.

10.5.1.2 Cell Suspension Cultures

Plant cell suspension cultures are often expedient technologies for large-scale biosynthesis of botanical extracts for use in cosmeceuticals. This technique of liquid suspensions is being continuously utilized for the commercial production of plant extracts by cosmetic manufacturers. Geraniol, a monoterpenoid for fragrance industries, has been acquired plentifully from cell suspension cultures (Chen and Viljoen 2010). Liquid cultures have formed the source for the synthesis of a hydrosoluble cosmetic ingredient from tomato, *Lycopersicon esculentum*, with enhanced concentrations of active principles like flavonoids and phenolic acids including rutin, coumaric acid, protocatechuic acid, and chlorogenic acid (Tito et al. 2011).

Anthocyanin pigments isolated from natural sources especially plants have much prospects in cosmeceutical industry wherein they could be used as UV protectors and anticancer agents owing to their high antioxidant property. Ananga et al. (2013) in their publication elaborate on how plant tissue culture has been put to use for synthesizing the natural pigment anthocyanin from grape cell suspension culture. The study revealed the potential of metabolic engineering alongside bioengineering of grape cell suspension cultures for scaling up the commercial production of natural anthocyanin with appropriate modifications in the bioreactor designs. The economic benefits and feasibility of using cell suspension culture of grapes for scaling up anthocyanin production was well demonstrated by a two-stage cultivation process of grape cell suspension in bioreactor (Cormier et al. 1996; Ananga et al. 2013).

Being a sustainable and consistent productive system, plant cell suspension cultures have been put to use for the bioproduction of active metabolites from botanicals with skin moisturizing capacity. Liquid suspension cultures from *Rubus idaeus* leaves were used to develop an oil-soluble extract abundant in essential fatty acids with increased hydration and moisturizing efficacy (Tito et al. 2015). The extracts induced expression of aquaporin 3, filaggrin, involucrin, and hyaluronic acid, which are the important genes involved in skin hydration and moisturization when introduced into cultures of keratinocytes and fibroblasts (Zappelli et al. 2016). Clinical validation gave convincing results with significant short-term and long-term hydrating effect keeping skin well moisturized upon application.

10.5.1.3 Stem Cell/Meristem Cell Cultures

Plant stem cell has been found to be good sources of metabolites. Morus et al. (2014) upon culturing these cells yielded pigments such as safflower and saflorin from *C. tinctorius*. Substantial protection from heavy metal toxicity has been exhibited by stem cell cultures of tomato, *L. esculentum*. Recent reports on advancement in stem cell cultures have proved that higher contents of metal chelating agents like phytochelatins and antioxidant molecules capable of scavenging metals could be produced from tomato stem cell extracts (Tito et al. 2011). The efficacy of this cosmetic active product to preserve nuclear DNA integrity and neutralize the heavy metal-induced degradation of collagen by inhibiting collagenase expression has been demonstrated. The cosmetic formulation in turn could induce collagen synthesis.

Cambial meristem cell cultures were shown to help amend many of the technical shortcomings of cell culture-based metabolite synthesis. This was shown by the production of ginsenosides from cambial meristematic cells enabling the commercial production of the metabolite (Ochoa-Villarreal et al. 2015). Wu and Zhong (1999) developed methods for the production of ginseng and the bio-active compounds from *P. ginseng* using plant cell culture. Ginseng and its active compounds are ascertained beneficial components for skin care products (Kim 2015; Shin et al. 2017; Yang et al. 2017). Compound K, a ginsenoside from *P. ginseng*, was proved to have antiaging properties under UVB irradiation pointing to its increased interest in cosmetic industry (Kim et al. 2018).

Meristem cell culture of *Buddleia davidii* has been utilized as an effective biofactory for the production of verbascoside (Zappelli et al. 2016). An anti-inflammatory phenylpropanoid glycoside, verbascoside, in a dose-dependent manner could effectively decrease the expression of the pro-inflammatory chemokine IL-8 on primary cultures of human keratinocytes stimulated by tumor necrosis factor alpha (TNF-α) (Pastore et al. 2009). TNF-α is a cytokine involved in the acute phase reaction in the systemic inflammation. Apart from its anti-inflammatory activity, verbascoside is known to show tremendous antioxidant properties (Vertuani et al. 2011) as well. Topical application of antioxidants has been proved to be one of the best approaches for dermal protection against oxidative damage especially those caused by UV radiation, exposure to ozone, and pollutants. Studies focusing on the molecular mechanisms of the biological activity of natural antioxidants of plant origin, especially the phenylpropanoids, have enticed the cosmetic manufacturers to include metabolites like verbascoside in cosmeceutical formulations with therapeutic application for modulating free radical-induced skin damage (Korkina 2007; Ranouille et al. 2017). Korkina et al. (2017) suggested the superiority of plant cell culture-derived metabolites over whole botanical extracts for topical photoprotection. Cosmeceutical preparations like sunscreen or post sun topical formulations could be made more effective by augmenting them with secondary metabolites derived from plant cell cultures elicited by a broadband UV light. Such formulations were found to be purest and extremely efficient photoprotectors (Potapovich et al. 2013). A recently published study by Kostyuk et al. (2018) has confirmed the efficacy of meristem plant cell cultures elicited with solar-simulating UV as the most environment-friendly viable biotechnological system leading to the production of polyphenols with photoprotective and antiaging properties. The above said examples and the advancements in plant stem cell research are opening up avenues for the formulation of skin care products which would cater to the personalized needs of consumers. Incorporating this science in the biosynthesis of topical application as well as developing a great understanding of the mechanism of action of key ingredients is the prudent approach to safe product development. This would be the futuristic stratagem to formulate skin care regimen which would deliver custom-made solutions based on unique skin types.

10.5.2 Genetic Transformation for the Metabolite Synthesis

An understanding about the key molecules involved in the metabolite pathway and the genes controlling the synthesis and their regulation will help manipulate the biosynthetic pathways for enhanced secondary metabolite production. A clear perception of the primary metabolic pathway and the molecules fed by the primary metabolism to generate secondary compounds will lead to the manipulation strategies for enhancing secondary metabolite biosynthesis. Utilizing cell cultures fed with intermediates and precursor molecules, considerable modifications can be made at points where the flux could be limiting (Jha 2007). However, even after successful transformation of target gene(s) into suitable host plant varieties, enrichment in accretion of metabolites is highly reliant on the regulatory factors. Hence, strategies have to be designed by trial and error method to enhance the accumulation of metabolites. By carefully selecting the right regulatory factors to go along with target genes and an accurate delivery system, metabolically engineered plants could be generated for obtaining useful phytocompounds. Even though cell cultures are a good target for genetic modifications leading to improved metabolite synthesis, their yield is highly affected by the characteristic tissue-specific expression and the degree of differentiation at cellular level. In plant species where the undifferentiated cell cultures are inefficient or of limited efficiency in metabolite synthesis, secondary metabolite production is enhanced in vitro by cellular differentiation either through organogenesis and embryogenesis or better through organ cultures including shoot and root cultures.

10.5.2.1 Hairy Root Cultures

An alternative technique to undifferentiated cell cultures which could be scaled up for industrial production of active phytochemicals is achieved by the induction of differentiated organ cultures. One of the best and effective systems in this regard is raising *Agrobacterium rhizogenes*-mediated hairy root cultures. *A. rhizogenes* is a gram-negative soil bacteria carrying a root-inducing (Ri) plasmid with T-DNA (transfer DNA), which holds specific genes for auxin and cytokinin synthesis. The bacteria commonly called the "natural genetic engineer" have the capacity to transfer the T- DNA to genome of plants which they infect (Guillon et al. 2006a; Ochoa-Villarreal et al. 2016) and inflict formation of hairy roots.

Besides being genetically stable, being independent of seasonal or geographic variations and special growth pattern, hairy roots are easy to establish and maintain in hormone-free medium. This type of cultures has high prospects for obtaining secondary metabolites especially those which are synthesized and (or) accumulated in plant roots. Many studies have reported the efficacy of hairy root cultures to produce phytochemicals at higher or comparable levels to the control plants (Srivastava and Srivastava 2007; Lee et al. 2010). In *P. ginseng* rhizomes, *A. rhizogenes* infection could enhance growth and elevate ginsenoside biosynthesis in hairy roots compared to the phytohormone treatment in normal roots. Rosmarinic acid production from *Ocimum basilicum* could be increased by threefold from hairy root cultures infected with *A. rhizogenes* (ATCC-15834). These examples, among the many, showcase the feasibility of using transformed hairy root cultures rather than untransformed normal roots for phytochemical synthesis (Tada et al. 1996; Pistelli et al. 2010).

Production of secondary metabolites with pharmaceutical, cosmeceutical, and nutraceutical use has been achieved through hairy root cultures of many plant species (Giri and Narasu, 2000; Guillon et al. 2006b; Park et al. 2008; Lee et al. 2010). Such cultures have been portrayed as a sustainable bioproduction technique for various natural products including nicotine, ginsenosides, camptothecin, tropane, and pyrrolizidine alkaloids (Wink et al. 2005; El Meskaoui 2013; Ochoa-Villarreal et al. 2016). Hairy root cultures of muscadine grape (*Vitis rotundifolia* Michx.) are used for the extracellular production of resveratrol (Nopo-Olazabal et al. 2013; Jeandet et al. 2016). Resveratrol, a stilbenoid derived from grape, is well known for its photoprotection properties against UV radiation-mediated oxidative stress and cutaneous damages including skin cancer (Ndiaye et al. 2011; Soto et al. 2015). This metabolite is a sought out supplement in many antiaging and skin care cosmetic products available in the market. A recent study by Sena et al. (2018) was a quest to identify whether the extract from hairy root cultures of *Brassica rapa* could be employed in skin whitening cosmeceutical formulations with added therapeutic ability to treat pigmentation disorders. Two preparations made from the extracts were tested for melanogenesis and expression of matrix proteins involved in correct pigment distribution. Tested on skin cell cultures and on human skin explants, both the hairy root extracts gave positive response. There was a substantial decrease in melanin synthesis, and the gene expression in melanin distribution was highly modulated. The synergistic effect of the two extracts showed hypopigmenting activity, thereby promising the efficacy of hairy root cultures as source of natural ingredients in skin care cosmeceuticals.

10.5.3 Scaling Up of Natural Product Production: Use of Bioreactors

Plant cell and tissue culture has become a promising alternative for the synthesis of phytocompounds which are biosustainable and contaminant-free. To obtain higher yield of metabolites for commercial exploitation, a bioprocess-based scaling up from a lab to pilot scale to factory scale has to be done. Large-scale cultivation of plant cells, which act as biofactories producing active metabolites, is made possible with bioreactors. In addition to the biomass scale-up, bioreactors have been found very helpful in the large-scale synthesis of secondary metabolites (Hussain et al. 2012). The scaling up of metabolite production by transferring the production of resveratrol from the laboratory to industrial scale has been achieved using cell suspensions in bioreactors (Jeandet et al. 2016).

Stirred tank reactors, airlift reactors, and bubble column reactors are some of the traditional bioreactor systems (which were primarily designed for microbial cultures) being utilized for the cultivation of plant cell cultures. Diversa (Ahrensburg, Germany), the world's largest plant cell culture facility, utilizes a cascade of five stirred tank bioreactors of varying capacities for mass production of target compounds (Georgiev et al. 2009). Barbulova et al. (2010) successfully utilized bioreactor for the culture of *Rubus idaeus*, wild red raspberry, for phytosynthesis of metabolite for cosmetic preparation. Nohynek et al. (2014) developed an in vitro system for the sustainable, large-scale production of cloudberry cells in stirred tank bioreactors. This cultivation process is presently in use for the industrial production of cloudberry (*R. chamaemorus*) cells for commercial cosmetic preparations. The authors suggested the possibility of applying the technique for scaled up production of cloudberry metabolites as well.

Selection of appropriate bioreactor system is of utmost importance to a successful commercial-level biosynthesis of metabolites. Plant cell cultures unlike the microbial cultures are highly sensitive to shear stress especially when cultured in stir tank bioreactors. Depending on the specific growth patterns of the plant cells and tissues, bioreactor design varies. Apart from the design, parameters like sucrose concentration (Hao and Guan 2012; Cui et al. 2014), speed of agitation (if stirred tanks are to be used), the density of inoculum (Shohael et al. 2014; Thanh et al. 2014), and rate of aeration (Murthy et al. 2014a) have to be optimized depending on the cultivated species or the cell lines used.

Yield of metabolite could vary depending on the bioreactor system used for cell culture. This is best depicted by the varied yield recorded for stilbene synthesis expressed as the resveratrol production in mg/g FW using a combination of elicitors. Cell suspensions of purple grapes variety Gamay yielded a maximum of

7.03 g/l resveratrol when cultured in a stirred tank bioreactor (Vera-Urbina et al. 2013). The yield from the cell suspension cultures of the same plant was only 6 g/l in a bubble column cylindrical bioreactor system (Almagro et al. 2013). At the same time, V-shaped bubble column reactor resulted in a yield of 3.3 g/l of resveratrol (Vera-Urbina et al. 2013). For increased biomass as well as accumulation of ginsenosides in the ginseng adventitious root cultures, balloon type of bioreactor was found beneficial than the other types of reactors (Kim et al. 2005; Murthy et al. 2014b).

Liquid suspension cultures are unique systems offering possibilities for large-scale bioreactor process. Nevertheless, the optimal bioreactor system for plant suspension culture differs from that of the tissue or organ cultures (Werner et al. 2017). Progress in bioprocess engineering has been a driving force in the designing of bioreactors congruent with the industrial scale-up of hairy root systems. Considering the specific growth pattern of hairy roots which are highly prone to shear stress, a specialized mist-based bioreactor was developed by ROOTec Bioactives Ltd. (Basel, Switzerland) especially for the phytosynthesis of valuable natural products through hairy root cultures (Ochoa-Villarreal et al. 2016).

Despite the challenges and variations in design and culture conditions, bioreactors have been in use for commercial synthesis of natural products to fulfil the needs of the pharmaceutical and cosmetic industry. CBN Biotech Company (South Korea) produces around 40–45 tons of ginseng adventitious roots per year using four 10,000 l capacity bioreactors. Likewise, Research Center for the Development of Advanced Horticultural Technology (RCDAHT), Chungbuk National University (South Korea), has isolated specific bio-active metabolites from various plants including *Echinacea purpurea*, *E. angustifolia*, *Hypericum perforatum*, *Eleutherococcus koreanum*, and *Morinda citrifolia* by bioreactor cultivation of adventitious roots (Lee et al. 2011a, b; Cui et al. 2013; Murthy et al. 2014b). All these examples are conspicuous applications of plant biotechnology, especially plant cell and tissue culture and bioreactor technology, in the synthesis and scale-up of active metabolites of high significance.

10.5.4 Plant Tissue Culture and Industrial Production of Metabolites

Reviewing the history of plant tissue culture application for production of metabolites, we come across examples for plant tissue culture-based in vitro processes which have been successful in the industrial production of metabolites for the cosmetic industry (Chermahini et al. 2011). The production of shikonin from *Lithospermum erythrorhizon* (Fujita and Tabata, 1986) by Mitsui Petrochemical Industries, Japan, is one of the earliest success stories. Following this many more cosmetic companies ventured into the in vitro methods for the production of metabolites for cosmetic preparation. Production of arbutin – a skin whitening agent – from *Catharanthus roseus* is yet another in vitro based commercial production of metabolite by Mitsui Petrochemical Industries, Japan (Yokoyama and Yanaigi 1991;

Misawa1994; Chermahini et al. 2011). Likewise, a cosmetic company from Japan, Kibun, has formulated in vitro plant tissue culture technique for mass production of the cosmetic pigment carthamin from *Carthamus tinctorius* (Yamamoto et al. 2002; Haghbeen 2006). The commercial companies utilizing plant cell culture and hairy root culture technologies for the biosynthesis of natural products for effective and safe cosmeceuticals are on the rise (Table 10.2). The number of patents related to natural segment for the food, pharmaceutical, and cosmetic products by such technologies has crossed the 25,000 mark and is still rapidly escalating. There are a multitude of cosmeceutical products launched by companies which points to the commercial feasibility of using plant metabolites from in vitro grown cells. Grape cell-derived liposomes formed one of the key ingredients in the beauty cream, "PhytoCellTec" launched by Mibelle Biochemistry (Switzerland), which also acts as strong UV protector capable of delaying photoaging. "Stem cell acne cream" marketed by Emerge Labs, New York, is augmented with the multifaceted natural product – verbascoside extracted from cell cultures of lilac, *Syringa vulgaris* (SpecialChem 2012). This antiaging cream claims to reduce acne by 40% within a month of use and substantially reduces redness and inflammation of the skin. "Resistem™" is yet another cosmeceutical product developed by a French company, Sederma, containing anthocyanin pigments of grape cell suspension cultures (Ananga et al. 2013).

Mibelle Biochemistry developed a liposomal preparation "PhytoCellTec™ *Malus Domestica*" from stem cells of a rare apple cultivar, *Malus domestica* cultivar 'Uttwiler Spätlauber', using callus cells produced in a bioreactor (Blum et al. 2013). This technology patented in the USA (US 9,155,916 B2/US 8,580,320 B2) and in

Table 10.2 Plant tissue culture-derived natural products used in cosmeceutical industry

Plant name	Metabolite	Culture type	Manufacturer	References
Lithospermum erythrorhizon	Shikonin	Cell culture	Mitsui Petrochemical Industries, Japan	Fujita and Tabata (1986)
Catharanthus roseus	Arbutin	Cell culture	Mitsui Petrochemical Industries, Japan	Misawa (1994); Chermahini et al. (2011)
Carthamus tinctorius	Carthamin	Cell culture	Kibun, Japan	Chermahini et al. (2011)
Vitex vinifera	Anthocyanin	Cell suspension-derived liposome	Mibelle Biochemistry (Switzerland)	Ananga et al. (2013)
Panax ginseng Wild ginseng	Ginseng	Cell culture	Unhwa Biotech Corp., Jeonbuk, South Korea	Ochoa-Villarreal et al. (2016)
Panax ginseng	Ginsenosides	Hairy root	ROOTec, Witterswil, Switzerland	
Atropa belladonna	Atropine	Hairy root	ROOTec, Witterswil, Switzerland	
Nicotiana glauca	Nicotine	Hairy root	ROOTec, Witterswil, Switzerland	

Korea (10–1,470,632) was the first-ever plant stem cell-based ingredient to hit the cosmetic market. “PhytoCellTec™ *Malus Domestica*” is now being used by the cosmetic giants for the preparation of topical formulations in many of their antiaging skin care and hair care products. A series of skin care formulations including antiaging serum, lightening cream, lightening cleanser, and lotion has been launched by Image Skincare utilizing plant stem cell technology. Stem cells from gardenia, echinacea, lilac, and orange are advertised to be key ingredients of stem cell products like “DermaQuest,” “Stem Cell 3D,” “HydraFirm Serum,” and “Peptide Eye Firming Serum” (Trehan et al. 2017).

10.6 Cosmeceuticals: Regulatory Policies and Legislations

Cosmeceuticals, the fancy name given to cosmetic formulations which also have a therapeutic (medical or drug-like) activity, is legally not valid under any of the cosmetic or drug regulations or acts approved collectively across the globe. However, the terminology in modern days is used extensively in describing the products which are neither a cosmetic nor a drug in the true sense but falls in the borderline between the two – cosmetics and pharmaceuticals (Dureja et al. 2005; Ligade and Udupa, 2010). Normally used like a topical product in the form of a cream, powder, or lotion, cosmeceuticals have taken its place in the skin care routine. They are being used for improving texture, fine lines, pigmentation, and protection against photoaging. They do not need a prescription and is easily available over the counter.

Regulations governing the cosmeceuticals are very difficult in the wake that they are not yet recognized by agencies like Food and Drug Administration (FDA) or Federal Food, Drug, and Cosmetic Act (FD&C Act). Topical products are classified differently in different countries, and there is no consensus between Asia, Europe, America, and other countries regarding the cosmeceutical regulations (Bijauliya et al. 2017). Countries like Europe and the USA do not acknowledge these products and categorize them as either drugs or cosmetics. These two are defined very specifically and are bound by different laws and regulations. Drugs are defined as “medicines for internal or external use of human beings or animals and all substances intended to be used for; or in the diagnosis, treatment, mitigation or prevention of any disease or disorder in humans or animals” by Drugs and Cosmetic Act of 1940. Cosmetics are defined as “any article intended to be rubbed, poured, sprinkled or sprayed on or introduced into or applied to any part of the human body for cleansing, beautifying, promoting attractiveness or altering the appearance and includes any article intended for use as a component of cosmetic” (Joshi and Pawar 2015; Jain 2016). Even though FDA has not recognized cosmeceuticals, the claims for the therapeutic efficacy of such products are under the review of the agency. This is mandatory for its approval as a therapeutic agent. However, cosmetics do not require any mandatory review by the FDA (Bijauliya et al. 2017).

Formulations which are cosmetic/drug combinations (anti-dandruff shampoo, sunscreen moisturizers, antiperspirant deodorants, anticavity toothpaste with fluorides, etc.) are distinguished under three categories: cosmetic products, functional (quasi-drug) cosmetics, and drugs by Korea and Japan. At present only these two countries have legislation regarding cosmeceutical products. While Thailand calls such formulations as "controlled cosmetics," they are known as "cosmetic-type drugs" in Hong Kong (Bijauliya et al. 2017). In Europe, sunscreens, anti-dandruff shampoos, and deodorants with antiperspirants are marketed as cosmetics. The same products are regulated as drugs in the USA (Bakkali et al. 2008).

Similar category products are under varied regulations in different nations which bring much apprehension to the consumers. In certain countries the products are registered as drugs, while in some other countries, they are termed cosmetics and cosmeceuticals. The therapeutic claim of such products will become valid only when the product is approved by the FDA or equivalent agency. However, careful labelling of cosmeceuticals which are not intended to be regulated as drugs by FDA will be conducive to avoid castigatory action by the US Federal Trade Commission. If a claim regarding the therapeutic property is made for a product, the manufacturer has the responsibility to corroborate the claim through scientific validation. To ensure no deceptive and misleading claims are done by the manufacturers, advertising of cosmetics is regulated under the Federal Trade Commission (FTC) Act. Hence to legally market the cosmeceutical products, cosmetic manufacturers should comply with FDA regulations and FTC advertising Act.

Presently, cosmeceuticals have become popular among skin care regime. They are likely to hold a significant position in therapeutic advancements in the near future. Synchronization of cosmetics and drug formulations between different countries would bring more consensus regarding the categorization of cosmeceuticals (Aziz et al. 2017). Stringent rules and legislations for regulating the purity, safety, and efficacy of the cosmeceutical products should be formulated. Quality control of the cosmetic products should be given predominance. All these together will offer the customers the flexibility to choose the right cosmetic product which suits personal requirements with a complete knowledge about the precise ingredients that make up the formulation.

10.7 Conclusion and Future Prospective

Although not a recognized term among drugs and cosmetic approving agencies worldwide, cosmeceuticals hold a prime position in cosmetic market with a CAGR increase of 4.7% from 2012 to 2017. It is expected to rise to 5.95% by 2017–2022. According to a global market analysis report, cosmeceutical products will reach approximately 42 billion dollar demand in the world and will lead the cosmetic industry in the near future (Lohani et al. 2014). There are various factors nurturing the pace of cosmeceutical industry which include increased interest to youthful and radiant appearance, awareness about safer side of natural products compared to artificial cosmetic enhancers, research and development of novel cosmeceutical products, enhanced drug delivery modalities, and scientific awareness on mode of action of cosmeceutical products. The range of new products launched under the cosmeceutical category in recent years is an ample proof validating its consumer demand.

Skin care cosmeceuticals are the most sought class of its kind holding around 62% of product category. Natural products isolated from plants, marine organisms, and other sources like honey bee, mollusks, and insects are widely used in antiaging, antioxidant, UV protectant, and fairness-enhancing cosmetic formulations. Increased acceptance of natural products and proven efficacy played substantial role in the boost up of industry at present. The development of novel formulations from cosmetic giants is at par with ever-growing demand of luxury cosmeceuticals. Opportunities are everlasting in the field of phytopharmacology and pharmacotherapeutics as the nature holds the treasure of medicinally active compounds that cure maladies and render charisma.

References

Abbasi AM, Khan MA, Ahmad M, Zafar M, Jahan S, Sultana S (2010) Ethnopharmacological application of medicinal plants to cure skin diseases and in folk cosmetics among the tribal communities of North-West Frontier Province Pakistan. J Ethnopharmacol 128:322–335

Almagro L, Belchi-Navarro S, Sabater-Jara S, Vera-Urbina JC, Selles-Marchart S, Bru R, Pedreno MA (2013) Bioproduction of trans -resveratrol from grapevine cell cultures. In: Ramawat KG, Mérillon JM (eds) Handbook of natural products. Springer, Berlin/Heidelberg, pp 1683–1713

Ananga A, Georgiev V, Ochieng J, Phills B, Tsolova V (2013) Production of anthocyanins in grape cell cultures: a potential source of raw material for pharmaceutical, food, and cosmetic industries, the mediterranean genetic code barbara sladonja. Intech Open. https://doi.org/10.5772/54592

Anthonavage MMS, Saliou C, Tucker-Samaras S, Zedayko T (2011) Clinical benefits of topical application of *Artemisia abrotanum* L. (southern wood) on photo-damaged skin. J Am Acad Dermatol 64:22

Aranaz I, Acosta N, Civera C, Elorza B, Mingo J, Castro C, Gandia MDL, Caballero AH (2018) Cosmetics and cosmeceutical applications of chitin, chitosan and their derivatives. Polymers 10:213

Archana G, Sabina K, Babuskin S, Radhakrishnan K, Fayidh MA, Babu AS, Sivarajan M, Sukumar M (2013) Preparation and characterization of mucilage polysaccharide for biomedical applications. Carbohydr Polym 98:89–94

Ash M, Ash I (2007) In: Ash M (ed) Handbook of fillers, extenders, and diluents. Synapse Information resources, New York, pp 238–249

Asia Personal Care and Cosmetics Market Guide (2016) U.S. Commercial Service and Industry & Analysis (I&A). www.trade.gov/industry/materials/AsiaCosmetics MarketGuide.pdf; Accessed 18 Sept 2018

Aziz AA, Taher ZM, Muda R, Aziz R (2017) Cosmeceuticals and natural cosmetics. In: Hasham R (ed) Recent trends in research into Malaysian medicinal plants research. Penerbit UTM Press, Malaysia, pp 126–175

Bakkali F, Averbeck S, Averbeck D, Idaomar M (2008) Biological effects of essential oils-A review. Food Chem Toxicol 46:446–475

Banka N, Bunagan MJ, Shapiro J (2013) Pattern hair loss in men: diagnosis and medical treatment. Dermatol Clin 31:129–140

Bansal M, Manchanda K, Pandey SS (2012) Role of caffeine in the management of androgenetic alopecia. Int J Trichology 4:185–186

Barbulova A, Tito A, Carola A, Bimonte M, de Laurentis F, D'Ambrosio P, Apone F, Colucci G, Monoli I, Cucchiara M, Hill J (2010) Raspberry stem cell extract to protect skin from inflammation and oxidative stress. Cosmet Toilets 125:38–47

Bijauliya RK, Alok S, Kumar M, Chanchal DK, Yadav S (2017) A comprehensive review on herbal cosmetics. Int'l J Pharm Sci Res 8:4930–4949

Birtić S, Dussort P, Pierre F-X, Bily AC, Roller M (2015) Carnosic acid. Phytochemistry 115:9–19

Blum P, Schurch C, Schmid D, Zuli F (2013) Cosmetic preparation and method for preparing the same. US Patent No. US8580320B2

Botla KMCVS, Rao UM, Rao KS (2013) Commercial importance of marine micro algae. Seaweed Res Utiln 35:118–128

Bowe WP, Pugliese S (2014) Cosmetic benefits of natural ingredients. J Drugs Dermatol 13:1021–1025

Burke KE (2015) Anti aging regimens. In: Draelos ZD (ed) Cosmetic dermatology- products and procedures, 2nd edn. Wiley Blackwell, Oxford, pp 492–500

Calabrese V, Scapagini G, Catalano C, Dinotta F, Geraci D, Morganti P (2000) Biochemical studies of a natural antioxidant isolated from rosemary and its application in cosmetic dermatology. Int J Tissue React 22:5–13

Carrier DR, Deban SM, Otterstrom J (2002) The face that sank the Essex: potential function of the spermaceti organ in aggression. J Exp Biol 205:1755–1763

Castelo-Soccio LA (2012) Hair manifestations of systemic disease. Curr Probl Pediatr Adolesc Health Care 42:198–203

Chao LK, Hua KF, Hsu HY, Cheng SS, Lin IF, Chen CJ, Chen ST, Chang ST (2008) Cinnamaldehyde inhibits pro-inflammatory cytokine secretion from monocytes macrophages through suppression of intracellular signaling. Food Chem Toxicol 46:220–231

Chen W, Viljoen AM (2010) Geraniol-A review of a commercially important fragrance material. South Afr J Bot 76:643–651

Chermahini SH, Majid FAA, Sarmidi MR (2011) Cosmeceutical value of herbal extracts as natural ingredients and novel technologies in anti-aging. J Med Plant Res 5:3074–3077

Chon SH, Tannahill R, Yao X, Southall MD, Pappas A (2015) Keratinocyte differentiation and upregulation of ceramide synthesis induced by an oat lipid extract via the activation of PPAR pathways. Exp Dermatol 24:290–295

Corinaldesi C, Barone G, Marcellini F, Anno AD, Danovaro R (2017) Marine microbial derived molecules and their potential use in cosmeceutical and cosmetic products. Mar Drugs 15:118

Cormier F, Brion F, Do CB, Moresoli C (1996) Development of process strategies for anthocyanin-based food colorant production using *Vitis vinifera* cell cultures. In: DiCosmo F, Misawa M (eds) Plant cell culture secondary metabolism toward industrial application. CRC Press LLC, Boca Raton, pp 167–186

Cornaghi L, Arnaboldi F, Calo R, Landoni F, Baruffaldi PWF, Marabini L, Donetti E (2016) Effects of UV rays and thymol/*Thymus vulgaris* L. extract in an *ex vivo* human skin model: morphological and genotoxicological assessment. Cells Tissues Organs 201:180–192

Cui HY, Baque MA, Lee EJ, Paek KY (2013) Scale-up of adventitious root cultures of *Echinacea angustifolia* in a pilot-scale bioreactor for the production of biomass and caffeic acid derivatives. Plant Biotechnol Rep 7:297–308

Cui XH, Murthy HN, Paek KY (2014) Production of adventitious root biomass and bioactive compounds from *Hypericum perforatum* L. though large scale bioreactor cultures. In: Paek KY, Murthy HN, Zhong JJ (eds) Production of biomass and bioactive compounds using bioreactor technology. Springer, Dordrecht, pp 251–284

Deshmukh SS, Katare YS, Shyale SS, Bhujbal SS, Kadam SD, Landge DA, Shah DV, Pawar JB (2013) Isolation and evaluation of mucilage of *Adansonia digitata* Linn. as a suspending agent. J Pharm 2013:379750. https://doi.org/10.1155/2013/379750

Deters AM, Lengsfeld C, Hensel A (2005) Oligo and polysaccharides exhibit a structure-dependent bioactivity on human keratinocytes *in vitro*. J Ethnopharmacol 102:391–399

Donnez D, Jeandet P, Clement C, Courot E (2009) Bioproduction of resveratrol and stilbene derivatives by plant cells and microorganisms. Trends Biotechnol 27:706–713

Dureja H, Kaushik D, Gupta M, Kumar V, Lather V (2005) Cosmeceuticals: an emerging concept. Indian J Pharmacol 37:155–159

Ediriweera ERHSS, Premarathna NYS (2012) Medicinal and cosmetic uses of bee's honey- a review. Ayu 33:178–182
El Meskaoui A (2013) Plant cell tissue and organ culture biotechnology and its application in medicinal and aromatic plants. Med Aromat Plants 2:147
El-Bashier ZM, Fouad MA (2002) A preliminary pilot study on head lice pediculosis in Shakaria Governorate and treatment of lice with natural plant products. J Egypt Soc Parasitol 32:725–776
Elias PM, Friend DS (1975) The permeability barrier in mammalian epidermis. J Cell Biol 65:180–191
F'guyer S, Afaq F, Mukhtar H (2003) Photochemoprevention of skin cancer by botanical agents. Photodermatol Photoimmunol Photomed 19:56–72
Fan DL, Zhao WJ, Wang YX, Han SY, Guo S (2012) Oxymatrine inhibits collagen synthesis in keloid fibroblasts via inhibition of transforming growth factor-β1/Smad signaling pathway. Int J Dermatol 51:463–472
Farris PK (2010) Natural ingredients and their applications in dermatology. In: Kinnie PA (ed) Practical dermatology. Rick Ehrlich, New York, pp 51–54
Feng S, Luo Z, Tao B, Chen C (2015) Ultrasonic-assisted extraction and purification of phenolic compounds from sugarcanes (*Saccharum officinarum* L.) rinds. Food Sci Technol-LEB 60:970–976
Fischer TW, Hipler UC, Elsner P (2007) Effect of caffeine and testosterone on the proliferation of human hair follicles *in vitro*. Int J Dermatol 46:27–35
Fischer R, Vasilev N, Twyman RM, Schillberg S (2015) High-value products from plants: the challenges of process optimization. Curr Opin Biotechnol 32:156–162
Fujita Y, Tabata M (1986) Secondary metabolites from plant cells. In: Proceedings of 6th international congress of plant tissue and cell culture. IAPTC, Minneapolis
Furukawa H, Hayashi A, Limura T (2012) Copolymer having carbosiloxane dendrimer structure and hydrophilic group. US Patent No. US9670301B2
Ganesan P, Choi D (2016) Current application of phytocompound-based nanocosmeceuticals for beauty and skin therapy. Int J Nanomedicine 11:1987–2007
Gao SL, Zhu DN, Cai ZH, Jiang Y, Xu DR (2004) Organ culture of a precious Chinese medicinal plant – *Fritillaria unibracteata*. Plant Cell Tissue Organ Cult 59:197–201
Geetha RV, Roy A (2012) *In vitro* evaluation of antibacterial activity of ethanolic root extract of *Glycyrrhiza glabra* on oral microbes. Int'l J Drug Dev 4:161–165
Georgiev MI, Weber J, Maciuk A (2009) Bioprocessing of plant cell cultures for mass production of targeted compounds. Appl Microbiol Biotechnol 83:809–823
Giri A, Narasu MJ (2000) Transgenic hairy roots: recent trends and applications. Biotechnol Adv 18:1–22
Global Cosmeceutical Market 2017–2021 (2016). www.technavio.com/report/global-cosmetics-and-toiletry-global-cosmeceuticals-market-2017-2021; Accessed 18 Sept 2018
Golubovic-Liakopoulos N, Simon SR, Shah B (2011) Nanotechnology use with cosmeceuticals. Semin Cutan Med Surg 30:176–180
Green BA (2014) Cosmeceutical uses and benefits of alpha, poly and bionic hydroxy acids. In: Farris PK (ed) Cosmeceuticals and cosmetic practice. Wiley, London, pp 69–80
Green BA, Van Scott EJ, Yu RJ (2016) Clinical use of hydroxyl acids. In: Draelos ZD (ed) Cosmetic dermatology- Products and procedures, 2nd edn. Wiley Blackwell, London, pp 346–356
Guillon S, Trémouillaux-Guiller J, Pati PK, Rideau M, Gantet P (2006a) Hairy root research: recent scenario and exciting prospects. Curr Opin Plant Biol 9:341–346
Guillon S, Tremouillaux-Guiller J, Pati PK, Rideau M, Gantet P (2006b) Harnessing the potential of hairy roots: dawn of a new era. Trends Biotechnol 24:403–409
Gülseren I, Corredig M (2013) Storage stability and physical characteristics of tea-polyphenol-bearing nanoliposomes prepared with milk fat globule membrane phospholipids. J Agric Food Chem 61:3242–3251
Guo S, Ge Y, Jom KN (2017) A review of phytochemistry, metabolite changes, and medicinal uses of the common sunflower seed and sprouts (*Helianthus annuus* L.). Chem Cent J 11:95

Haberlandt G (1902) Culturversuche mit isolierten Pflanzenzellen. Sitzungsberichte Math. Naturw Kl Kais Akad Wiss Wien 111:69–92

Haghbeen K (2006) *Lithospermum officinale* callus produces shikalin. Bologia 61:463–467

Hamman HJ (2008) Composition and applications of *Aloe vera* leaf gel. Molecules 13:1599–1616

Han SB, Kwon SS, Jeong YM, Yu ER, Park SN (2014) Physical characterization and *in vitro* skin permeation of solid lipid nanoparticles for transdermal delivery of quercetin. Int J Cosmet Sci 36:588–597

Hao JP, Guan Q (2012) Synthesis of saikosaponins in adventitious roots of *Bupleurum chinense* by semi-continuous culture. Plant Cell Tissue Organ Cult 108:159–165

Herman A, Herman AP (2016) Mechanism of action of herbs and their active constituents used in hair loss treatment. Fitotherapia 114:18–25

Ho D, Jaqdeo J, Waldorf HA (2016) Is there a role for arnica and bromelain in prevention of post-procedure ecchymosis or edema: a systematic review of the literature. Dermatol Surg 42:445–463

Huber C, Christopher E (1977) Keratolytic effect of salicylic acid. Arch Dermatol Res 257:293–298

Hussain MS, Fareed S, Ansari S, Rahman MA, Ahmad IZ, Saeed M (2012) Current approaches toward production of secondary plant metabolites. J Pharm Bioallied Sci 4:10–20

Hwang E, Park SY, Yin CS, Kim HT, Kim YM, Yi TH (2017) Antiaging effects of the mixture of *Panax ginseng* and *Crataegus pinnatifida* in human dermal fibroblasts and healthy human skin. J Ginseng Res 41:69–77

Idris ED, Khalid N, Ibrahim H, Annuar MSM (2007) Production of Zerumbone from *in vitro* derived rhizome of *Zingiber zerumbet* for pharmaceutical and cosmeceutical industry. In: 12th biological sciences graduate congress, 17–19th December, 2007 University of Malaya, Malaysia, p 227

Jadoon S, Karim S, Asad MHB, Akram MR, Khan AK, Malik A, Chen C, Murtaza G (2015) Anti-aging potential of phytoextract loaded–pharmaceutical creams for human skin cell longevity. Oxidative Med Cell Longev 2015:709628. https://doi.org/10.1155/2015/709628

Jain NK (2016) In: Jain MK (ed) A textbook of forensic pharmacy. Vallabh Prakashan, Delhi

Jeandet P, Vasserot Y, Chastang T, Courot E (2013) Engineering microbial cells for the biosynthesis of natural compounds of pharmaceutical significance. Biomed Res Int 2013:780145. https://doi.org/10.1155/2013/780145

Jeandet P, Clément C, Tisserant L, Crouzet J, Courot E (2016) Use of grapevine cell cultures for the production of phytostilbenes of cosmetic interest. C R Chim 19:1062–1070

Jha S (2007) Genetic transformation for production of secondary metabolites. In: Ramawat KG, Merillon JM (eds) Biotechnology, secondary metabolites-plants and microbes, 2nd edn. CRC Press/Taylor and Francis Group, Boca Raton, pp 297–332

Joshi LS, Pawar HA (2015) Herbal cosmetics and cosmeceuticals: an overview. Nat Prod Chem Res 3:170

Juliano C, Magrini GA (2018) Cosmetic functional ingredients from botanical sources for anti-pollution skincare products. Cosmetics 5:19

Juliano C, Mattana A, Usai M (2000) Composition and *in vitro* antimicrobial activity of the essential oil of *Thymus herba-barona* Loisel growing wild in Sardinia. J Essent Oil Res 12:516–552

Kapoor M, Si S (2014) Strategic analysis of cosmeceuticals with special reference to antiaging creams. Int J Business and Management Inv 3:44–52

Karuppusamy S (2009) A review on trends in production of secondary metabolites from higher plants by *in vitro* tissue, organ and cell cultures. J Med Plants Res 3:1222–1239

Katz LM, Dewan K, Bronaugh RL (2015) Nanotechnology in cosmetics. Food Chem Toxicol 85:127–137

Khan IA, Abourashed EA (2010) Leung's encyclopedia of common natural ingredients. Wiley, Hoboken

Kim K (2015) Effect of ginseng and ginsenosides on melanogenesis and their mechanism of action. J Ginseng Res 39:1–6

Kim YS, Hahn EJ, Shin CY, Paek KY (2005) Effects of aeration and sparger type on growth and ginsenoside accumulation in bioreactor cultures of ginseng adventitious root (*Panax ginseng* C.A. Meyer). Korean J Plant Biotechnol 32:111–116

Kim J, Lee KW, Lee HJ (2011) Cocoa (*Theobroma cacao*) seeds and phytochemicals in human health. In: Preedy VR, Watson RR, Patel BV (eds) Nuts and seeds in health and disease prevention. Elsevier Inc, Burlington, pp 351–360

Kim E, Kim D, Yoo S, Hong YH, Han SY, Jeong S, Jeong D, Kim J, Cho JY, Park J (2018) The skin protective effects of compound K, a metabolite of ginsenoside Rb1 from *Panax ginseng*. J Ginseng Res 42:218–224

Kitture R, Ghosh S, More PA, Date K, Gaware S, Datar S, Chopade BA, Kale SN (2015) Curcumin-loaded, self-assembled *Aloe vera* template for superior antioxidant activity and trans-membrane drug release. J Nanosci Nanotechnol 15:4039–4045

Kligman AM (2000) Cosmetics- A dermatologists look to the future: promises and problems. Dermatol Clin 18:699–709

Kong SZ, Shi XG, Feng XX, Li WJ, Liu WH, Chen ZW, Xie JH, Lai XP, Zhang XJ, Su ZR (2013) Inhibitory effect of hydroxysafflor yellow A on mice skin photoaging induced by UV irradiation. Rejuvenation Res 16:404–413

Korkina LG (2007) Phenylpropanoids as naturally occurring antioxidants: from plant defence to human health. Cell Mol Biol 53:15–25

Korkina L, Mayer W, De Luca C (2017) Meristem plant cells as a sustainable source of redox actives for skin rejuvenation. Biomol Ther 7:40

Kostyuk V, Potapovich A, Albuhaydar AR, Mayer W, Luca CD, Korkina L (2018) Natural substances for prevention of skin photoaging: screening systems in the development of sunscreen and rejuvenation cosmetics. Rejuvenation Res 21:91–101

Kumar T, Chaiyasut C, Rungseevijitprapa W, Suttajit M (2011) Screening of steroid 5α-reductase inhibitory activity and total phenolic content of Thai plants. J Med Plant Res 5:1265–1271

Kumari K, Sharma PK, Gupta R (2017) Nano-Cosmeceuticals: an emerging novel trend towards dermal care. Adv Cosmetics Dermatol 3:1–12

Kwack MH, Kim MK, Kim JC, Sung YK (2010) L-ascorbic acid 2-phosphate represses the dihydrotestosterone-induced dickkopf-1 expression in human balding dermal papilla cells. Exp Dermatol 19:110–112

Kwack MH, Kang BM, Kim MK, Kim JC, Sung YK (2011) Minoxidil activates beta-catenin pathway in human dermal papilla cells: a possible explanation for its anagen prolongation effect. J Dermatol Sci 62:154–159

Lee SY, Lee CY, Eom SH, Kim YK, Park NI, Park SU (2010) Rosmarinic acid production from transformed root cultures of *Nepeta cataria* L. Sci Res Essays 5:1122–1126

Lee EJ, Moh SH, Paek KY (2011a) Influence of inoculum density and aeration volume on biomass and bioactive compound production in bulb-type bioreactor cultures of *Eleutherococcus koreanum* Nakai. Bioresour Technol 102:7165–7170

Lee Y, Lee DE, Lee HS, Kim SK, Lee WS, Kim SH, Kim MW (2011b) Influence of auxins, cytokinins, and nitrogen on production of rutin from callus and adventitious roots of the white mulberry tree (*Morus alba* L.). Plant Cell Tissue Organ Cult 105:9–19

Lewis W (2017) Cosmeceuticals 2017, Prime 7. https://www.prime-journal.com/cosmeceuticals-2017/; Accessed 18 May 2018

Ligade VS, Udupa N (2010) Pharmaceuticals, cosmeceuticals and nutraceuticals: an overview of regulations. Career Publications, Nashik

Lohani A, Verma A, Joshi H, Yadav N, Karki N (2014) Nanotechnology based cosmeceuticals. ISRN Dermatol 2014:843687. https://doi.org/10.1155/2014/843687

Loizzo MR, Pacetti D, Lucci P, Nunez O, Menichini F, Frega NG, Tundis R (2015) *Prunus persica var. platycarpa* (Tabacchiera Peach): bioactive compounds and antioxidant activity of pulp, peel and seed ethanolic extracts. Plant Foods Hum Nutr 70:331–337

Lu H, Liu K (2003) Phytoliths of common grasses in the coastal environments of southeastern USA Estuarine. Coast Shelf Sci 58:587–600

Madnani N, Khan K (2013) Hair cosmetics. Indian J Dermatol Venereol Leprol 79:654–667

Mahendranath G, Venugopalan A, Parimalan R, Giridhar P, Ravishankar GA (2011) Annatto pigment production in root cultures of Achiote (*Bixa orellana* L.). Plant Cell Tissue Organ Cult 106:517–522

Majeed M, Bhat B, Anand S, Sivakumar A, Paliwal P, Geetha KG (2011) Inhibition of UV-induced ROS and collagen damage by *Phyllanthus emblica* extract in normal human dermal fibroblasts. J Cosmet Sci 62:49–56

Milbury PE, Chen CY, Dolnikowski GG, Blumberg JB (2006) Determination of flavonoids and phenolics and their distribution in almonds. J Agric Food Chem 54:5027–5033

Miralles P, Chisvert A, Salvador A (2015) Determination of hydroxytyrosol and tyrosol by liquid chromatography for the quality control of cosmetic products based on olive extracts. J Pharm Biomed Anal 102:157–161

Misawa M (1994) Plant tissue culture: an alternative for production of useful metabolites. FAO Agric Serv Bull:1–87

Mishra AK, Krishnapriya, Ramesh NV (2017) Therapeutic uses of bees wax in ayurveda and its physico chemical analyses. Int J Res Ayurveda Pharm 8:25

Mitani H, Ryu A, Suzuki T, Yamashita M, Arakane K, Koide C (2007) Topical application of plant extracts containing xanthine derivatives can prevent UV-induced wrinkle formation in hairless mice. Photodermatol Photoimmunol Photomed 23:86–94

Morteza-Semnani K, Saeedi M, Shahnavaz B (2003) Comparison of antioxidant activity of extract from roots of licorice (*Glycyrrhiza glabra* L.) to commercial antioxidants in 2% hydroquinone cream. J Cosmet Sci 54:551–558

Morus M, Baran M, Rost-Roszkowska M, Skotnicka-Graca U (2014) Plant stem cells as innovation in cosmetics. Acta Pol Pharm 71:701–707

Murthy HN, Lee EJ, Paek KY (2014a) Production of secondary metabolites from cell and organ cultures: strategies and approaches for biomass improvement and metabolite accumulation. Plant Cell Tissue Organ Cult 118:1–16

Murthy HN, Dandin VS, Paek KY (2014b) Tools for biotechnological production of useful phytochemicals from adventitious root cultures. Phytochem Rev 15:129–145

Naha PC, Mukherjee SP, Byrne HJ (2018) Toxicology of engineered nanoparticles: focus on poly(amidoamine) dendrimers. Int J Environ Res Public Health 15:338

Nanda S, Nanda A, Khar RK (eds) (2010) Cosmetic technology. Birla Publications, Delhi, pp 105–123

Ndiaye M, Philippe C, Mukhtar H, Ahmad N (2011) The grape antioxidant resveratrol for skin disorders: promise, prospects, and challenges. Arch Biochem Biophys 508:164–170

Neha R, Shabla M, Indi T, Evita T (2018) Efficacy of alimental components in an oral supplement for the treatment of hair fall, hair growth, skin and nail problems and role of hairvit plus in their composition upgradation. Int J Sci Res Pub 8:309–313

No YA, Kwon T, Park HM, Han HJ, Ji HJ, Huh Y, Kim BJ (2015) A hair growth-enhancing component of hydrolysate of human placenta: *in vitro* and *in vivo* assessments. J Clin Investigat Dermatol 3:5

Nohynek L, Bailey M, Tahtiharju J, Seppanen-Laakso T, Rischer H, Oksman-Caldentey H, Puupponen-Pimia R (2014) Cloudberry (*Rubus chamaemorus*) cell culture with bioactive substances: establishment and mass propagation for industrial use. Eng Life Sci 14:667–675

Nopo-Olazabal C, Hubstenberger J, Nopo-Olazabal L, Medina-Bolivar F (2013) Antioxidant activity of selected stilbenoids and their bioproduction in hairy root cultures of muscadine grape (*Vitis rotundifolia* Michx.). J Agric Food Chem 61:11744–11758

Nosov AM (2012) Application of cell technologies for production of plant derived bioactive substances of plant origin. Appl Biochem Microbiol 48:609–624

Ochoa-Villarreal M, Howat S, Jang MO, Kim IS, Jin Y, Lee E, Loake JG (2015) Cambial meristematic cells: a platform for the production of plant natural products. New Biotechnol 32:581–587

Ochoa-Villarreal M, Howat S, Hong SM, Jang MO, Jin Y, Lee E, Loake JG (2016) Plant cell culture strategies for the production of natural products. BMB Rep 49:149–158

Ogawa Y, Akamatsu M, Hotta Y, Hosoda A, Tamura H (2010) Effect of essential oils, such as raspberry ketone and its derivatives, on antiandrogenic activity based on *in vitro* reporter gene assay. Bioorg Med Chem Lett 20:2111–2114

Oktemer T, Ipci K, Muluk NB, Cingi C (2015) A pastille combining myrrh tincture, peppermint oil and menthol to treat the upper airway. ENT Updates 5:128–131

Olaharski AJ, Rine J, Marshall BL, Babiarz J, Zhang L, Verdin E, Smith MT (2005) The flavoring agent dihydrocoumarin reverses epigenetic silencing and inhibits sirtuin deacetylases. PLoS Genet 1:e77

Olejnik A, Goscianska J, Nowak I (2012) Significance of hyaluronic acid in cosmetic industry and aesthetic medicine. Chemik 66:129–135

Olshan AM, Kohut BE, Vincent JW, Borden LC, Delgado N, Qaqish J, Sharma NC, McGuire JA (2000) Clinical effectiveness of essential oil-containing dentifrices in controlling oral malodor. Am J Dent 13:C18–C22

Oricha BS (2010) Cosmeceuticals: a review. Afr J Pharm Pharmacol 4:127–129

Park SU, Uddin MR, Xu H, Kim YK, Lee SK (2008) Biotechnological applications for rosmarinic acid production in plant. Afr J Biotechnol 7:4959–4965

Park CM, Cho WC, Song YS (2014) TOP1 and 2 polysaccharides from *Taraxacum officinale* inhibit NF-kB mediated inflammation and accelerate Nrf2-induced antioxidative potential through the modulation of PI3K-Akt signaling pathway in RAW264.7 cells. Food Chem Toxicol 66:56–64

Pastore S, Potapovich A, Kostyuk V, Mariani V, Lulli D, De Luca C, Korkina L (2009) Plant polyphenols effectively protect HaCaT cells from ultraviolet C-triggered necrosis and suppress inflammatory chemokine expression. Ann N Y Acad Sci 1171:305–313

Patel VR, Dumancas GG, Kasi Viswanath LC, Maples R, Subong BJ (2016) Castor oil: properties, uses, and optimization of processing parameters in commercial production. Lipid Insights 9:1–12

Patzelt A, Knorr F, Blume-Peytavi U, Sterry W, Lademann J (2008) Hair follicles, their disorders and their opportunities. Drug Discov Today Dis Mech 5:173–181

Peng HY, Lin CC, Wang HY, Shih Y, Chou ST (2014) The melanogenesis alteration effects of *Achillea millefolium* L. essential oil and linalyl acetate: involvement of oxidative stress and the JNK and ERK signaling pathways in melanoma cells. PLoS One 9:e95186

Phetcharat L, Wongsuphasawat K, Winther K (2015) The effectiveness of a standardized rose hip powder, containing seeds and shells of *Rosa canina*, on cell longevity, skin wrinkles, moisture and elasticity. Clin Interv Aging 10:1849–1856

Pinelo M, Rubilar M, Sineiro J, Núñez MJ (2004) Extraction of antioxidant phenolics from almond hulls (*Prunus amygdalus*) and pine sawdust (*Pinus pinaster*). Food Chem 85:267–273

Pistelli L, Giovannini A, Ruffoni B, Bertoli A, Pistelli L (2010) Hairy root cultures for secondary metabolites production. In: Giardi MT, Rea G, Berra B (eds) Bio-farms for nutraceuticals: functional food and safety control by biosensors. Landes Bioscience and Springer Science Business Media, New York, pp 167–184

Potapovich AI, Kostyuk VA, Kostyuk TV, de Luca C, Korkina LG (2013) Effects of pre- and post-treatment with plant polyphenols on human keratinocyte responses to solar UV. Inflamm Res 62:773–780

Prajapati VD, Jani GK, Moradiya NG, Randeria NP, Nagar BJ, Naikwadi NN, Variya BC (2013) Galactomannan: a versatile biodegradable seed polysaccharide. Int J Biol Macromol 60:83–92

Prakash S, Shelke AU (2014) Role of Triphala in dentistry. J Indian Soc Periodontol 18:132–135

Prasad MN, Sanjay KR, Prasad DS, Vijay N, Kothari R, Swamy SN (2012) A review on nutritional and nutraceutical properties of sesame. J Nutr Food Sci 2:127

Raj V, Jain A, Chaudhary J (2012) *Prunus armeniaca* (Apricot): an overview. J Pharm Res 5:3964–3966

Ramose-Silva M, da Silva Carneiro SC (2007) Elderly skin and its rejuvenation: products and procedures for the aging skin. J Cosmet Dermatol 6:40–50

Ranouille E, Bony E, Renimel-Krolikiewicz I, Berthon J, Filaire E (2017) A Concentrated Mix of Verbascoside and Echinacoside Induces Whole Biological Photoprotection of Skin Tissue. Int Fed Soc Cosmet Chem Mag 3:155–160

Ranveer RC, Sahoo AK (2017) Bioactive constituents of kokum and its potential health benefits. Nutri Food Toxicol 1:236–244

Rao HJ (2012) Therapeutic applications of almonds (*Prunus amygdalus* L.): a review. J Clin Diagn Res 6:130–135

Rao SM, Ravishankar GA (2002) Plant cell cultures: chemical factories of secondary metabolities. Biotechnol Adv 20:101–153

Riangjanapatee P, Muller RH, Keck CM, Okonogi S (2013) Development of lycopene-loaded nanostructured lipid carriers: effect of rice oil and cholesterol. Pharmazie 68:723–731

Rigano L, Lionetti N (2016) Nanobiomaterials in galenic formulations and cosmetics. In: Grumezescu AM (ed) Nanobiomaterials in galenic formulations and cosmetics – applications of nanobiomaterials. Elsevier, Oxford, pp 121–148

Rivers JK (2008) The role of cosmeceuticals in antiaging therapy. Skin Therapy Lett 13:510

Rodríguez MIA, Barroso LGR, Sánchez ML (2018) Collagen: a review on its sources and potential cosmetic applications. J Cosmet Dermatol 17:20–26

Rondanelli M, Perna S, Peroni G, Guido D (2015) A bibliometric study of scientific literature in Scopus on botanicals for treatment of androgenetic alopecia. J Cosmet Dermatol 15:120–130

Saha R (2012) Cosmeceuticals and herbal drugs: practical uses. Int J Pharm Sci Res 3:59–65

Sandha GK, Swami VK (2009) Jojoba oil as an organic shelf stable standard oil-phase base for cosmetic industry. Rasayan J Chem 2:300–306

Sanguigno L, Minale M, Vannini E, Riccio GAR, Casapullo A, Monti MC, Riccio R, Formisano S, Renzo GD, Cuomo O (2015) Oligosaccharidic fractions derivedfrom *Triticum vulgare* extract accelerate tissue repairing processes in *in vitro* and *in vivo* models of skin lesions. J Ethnopharmacol 159:198–208

Saraf S, Chhabra SK, Kaur CD, Saraf S (2012) Development of photo-chemo protective herbs containing cosmetic formulations for improving skin properties. J Cosmet Sci 63:119–131

Sena LM, Zappelli C, Apone F, Barbulova A, Tito A, Leone A, Oliviero T, Ferracane R, Fogliano V, Colucci G (2018) *Brassica rapa* hairy root extracts promote skin depigmentation by modulating melanin production and distribution. J Cosmet Dermatol 17:246–257

Shin S, Lee J, Son D, Park D, Jung E (2017) Anti-Skin-Aging activity of a standardized extract from *panax ginseng* leaves *in vitro* and in human volunteer. Cosmetics 4:1–12

Shohael AM, Murthy HN, Paek KY (2014) Pilot-scale culture of somatic embryos of *Eleutherococcus senticosus* in airlift bioreactors for the production of eleutherosides. Biotechnol Lett 36:1727–1733

Siahaan EA, Pangestuti R, Munandar H, Kim SK (2017) Cosmeceuticals properties of sea cucumbers: prospects and trends. Cosmetics 4:26

Siriamornpun S, Kaisoon O, Meeso N (2012) Changes in colour, antioxidant activities and carotenoids (lycopene, β carotene, lutein) of marigold flower (*Tagetes erecta* L.) resulting from different drying processes. J Funct Foods 4:757–766

Smith WP (1996) Epidermal and dermal effects of topical lactic acid. J Am Acad Dermatol 35:388–391

Solimine J, Garo E, Wedler J, Rusanov K, Fertig O, Hamburger M, Atanssov I, Butterweck V (2016) Tyrosinase inhibitory constituents from a polephenol enriched fraction of rose oil distillation wastewater. Fitoterapia 108:13–19

Soto ML, Falqué E, Domínguez H (2015) Relevance of natural phenolics from grape and derivative products in the formulation of cosmetics. Cosmetics 2:259–276

SpecialChem (2012). https://cosmetics.specialchem.com/news/product-news/emerge-labs-launches-stem-cell-acne-cream-to-reduce-inflammation%2D%2Dredness-on-skin; Accessed 18 May 2018

Srivastava S, Srivastava AK (2007) Hairy root culture for mass- production of high-value secondary metabolites. Crit Rev Biotechnol 27:29–43

Sumiyoshi M, Kimura Y (2009) Effects of a turmeric extract (*Curcuma longa*) on chronic ultraviolet B irradiation-induced skin damage in melanin-possessing hairless mice. Phytomedicine 16:1137–1143

Suwannateep N, Wanichwecharungruang S, Fluhr J, Patzelt A, Lademann J, Meinke MC (2013) Comparison of two encapsulated curcumin particular systems contained in different formulations with regard to *in vitro* skin penetration. Skin Res Technol 19:1–9

Tada H, Murakam Y, Omoto T, Shimomura K, Ishimaru K (1996) Rosmarinic acid and related phenolics in hairy root cultures of *Ocimum basilicum*. Phytochemistry 42:431–434

Takahashi T, Kamimura A, Yokoo Y, Honda S, Watanabe Y (2001) The first clinical trial of topical application of procyanidin B-2 to investigate its potential as a hair growing agent. Phytother Res 15:331–336

Thanh NT, Murthy HN, Paek KY (2014) Optimization of ginseng cell culture in airlift bioreactors and developing the large-scale production system. Ind Crop Prod 60:343–348

Thibault PK, Wlodarczyk J, Wenck A (1998) A double-blind randomized clinical trial on the effectiveness of a daily glycolic acid 5% formulation in the treatment of photoaging. Dermatol Surg 24:573–577

Tito A, Carola A, Bimonte M, Barbulova A, Arciello S, de Laurentiis F, Monoli I, Hill J, Gibertoni S, Colucci G, Apone F (2011) A tomato stem cell extract containing antioxidant compounds and metal chelating factors protects skin cells from heavy metal-induced damages. Int J Cosmet Sci 33:543–552

Tito A, Bimonte M, Carola A, De Lucia A, Barbulova A, Tortora A, Colucci G, Apone F (2015) An oil-soluble extract of *Rubus idaeus* cells enhances hydration and water homeostasis in skin cells. Int J Cosmet Sci 37:588–594

Tortora GJ, Grabowski SR (2013) Principles of anatomy and physiology, 14th edn. Wiley, New York, pp 110–150

Trehan S, Michniak-Kohn B, Beri K (2017) Plant stem cells in cosmetics: current trends and future directions. Future Sci OA 3:FSO226

Uhoda E, Pierard-Franchimont C, Petit L, Pierard GE (2005) Hydroxyacids. In: Elsner P, Maibach HI (eds) Cosmeceuticals and active cosmetics: drugs versus cosmetics, Cosmetics science and technology series. Taylor and Francis group, Boca Raton, pp 95–148

Upadhyay S, Ghosh AK, Singh V (2012) Hair growth promotant activity of petroleum ether root extractof *Glycyrrhiza glabra* L. (Fabaceae) in female rats. Trop J Pharm Res 11:753–758

Vañó-Galván S, Camacho F (2017) New treatments for hair loss. Actas Dermosifiliogr 108:221–228

Vera-Urbina JC, Selles-Marchart S, Martinez-Esteso MJ, Pedreno MA, Martinez RB (2013) Production of grapevine cell biomass (*Vitis vinifera* L. Gamay) and resveratrol in custom and commercial bioreactors using cyclodextrins and methyl-jasmonate elicitors. In: Delmas D (ed) Resveratrol: source, production, and health benefits. Nova Science Publishers Inc, New York, pp 19–40

Verma V, Gautam SP, Devi R, Singh N, Harjaskaran, Singh L (2016) Cosmeceuticals: acclaiming its most fascinating position in personal care industry. Ind Res J Pharm Sci 3:506–518

Vertuani S, Beghelli E, Scalambra E, Malisardi G, Copetti S, Toso RD, Baldisserotto A, Manfredini S (2011) Activity and stability studies of Verbascoside, a novel antioxidant, in dermo-cosmetic and pharmaceutical topical formulations. Molecules 16:7068–7080

Viinanen A, Salokannel M, Lammintausta K (2011) Gum Arabic as a cause of occupational allergy. J Allergy 2011:841508. https://doi.org/10.1155/2011/841508

Wang W, Li N, Luo M, Zu Y, Efferth T (2012) Antibacterial activity and anticancer activity of *Rosmarinus officinalis* L. essential oil compared to that of its main components. Molecules 17:2704–2713

Wang Z, Feng Y, Ma L, Li X, Ding W, Chen X (2017) Hair growth promoting effect of white wax and policosanol from white wax on the mouse model of testosterone-induced hair loss. Biomed Pharmacother 89:438–446

Werner S, Maschke RW, Eibl D, Eibl R (2017) Bioreactor technology for sustainable production of plant cell-derived products. In: Pavlov A, Bley T (eds) Bioprocessing of plant *in vitro* systems. Springer, Cham, pp 1–20

Wilson SA, Roberts SC (2012) Recent advances towards development and commercialization of plant cell culture processes for the synthesis of biomolecules. Plant Biotechnol J 10:249–268

Wink M, Alfermann AW, Franke R, Wetterauer B, Distl M, Windhövel J, Krohn O, Fuss E, Garden H, Mohagheghzadeh A, Wildi E, Ripplinger P (2005) Sustainable bioproduction of phytochemicals by plant *in vitro* cultures: anticancer agents. Plant Genet Resour 3:90–100

Wisniewski JD, Ellis DL, Lupo MP (2014) Facial rejuvenation: combining cosmeceuticals with cosmetic procedures. Cutis 94:122–126

Wu J, Zhong JJ (1999) Production of ginseng and its bioactive components in plant cell culture: current technological and applied aspects. J Biotechnol 68:89–99

Yamamoto H, Zhao P, Yakazi K, Inoue K (2002) Regulation of lithospermic acid B and shikonin production in *Lithospermum erythrorhizon* cell suspension cultures. Chem Pharm Bull 50:1086–1090

Yang Y, Ren C, Zhang Y, Wu XD (2017) Ginseng: an non-negligible natural remedy for healthy aging. Aging Dis 8:708–720

Yen GC, Duh PD, Chang DY (2000) Antioxidant activity of anthraquinones and anthrone. Food Chem 70:437–441

Yokoyama M, Yanaigi M (1991) In: Komamine A, Misawa M, Dilosmo F (eds) Plant cell cultures in Japan. CMC Co., Tokyo, pp 79–91

Yutani R, Teraoka R, Kitagawa S (2015) Microemulsion using polyoxyethylene sorbitan trioleate and its usage for skin delivery of resveratrol to protect skin against UV-induced damage. Chem Pharm Bull 63:741–745

Zappelli C, Barbulova A, Apone F, Colucci G (2016) Effective active ingredients obtained through biotechnology. Cosmetics 3:39